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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	FEB 25	CA/CAPLUS - Russian Agency for Patents and Trademarks (ROSPATENT) added to list of core patent offices covered
NEWS	4	FEB 28	PATDPAFULL - New display fields provide for legal status data from INPADOC
NEWS	5	FEB 28	BABS - Current-awareness alerts (SDIs) available
NEWS	6	FEB 28	MEDLINE/LMEDLINE reloaded
NEWS	7	MAR 02	GBFULL: New full-text patent database on STN
NEWS	8	MAR 03	REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS	9	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS	10	MAR 22	KOREAPAT now updated monthly; patent information enhanced
NEWS	11	MAR 22	Original IDE display format returns to REGISTRY/ZREGISTRY
NEWS	12	MAR 22	PATDPASPC - New patent database available
NEWS	13	MAR 22	REGISTRY/ZREGISTRY enhanced with experimental property tags
NEWS	14	APR 04	EPFULL enhanced with additional patent information and new fields
NEWS	15	APR 04	EMBASE - Database reloaded and enhanced
NEWS	16	APR 18	New CAS Information Use Policies available online
NEWS	17	APR 25	Patent searching, including current-awareness alerts (SDIs), based on application date in CA/CAplus and USPATFULL/USPAT2 may be affected by a change in filing date for U.S. applications.
NEWS	18	APR 28	Improved searching of U.S. Patent Classifications for U.S. patent records in CA/CAplus
NEWS	19	MAY 23	GBFULL enhanced with patent drawing images
NEWS	20	MAY 23	REGISTRY has been enhanced with source information from CHEMCATS
NEWS	21	MAY 26	STN User Update to be held June 6 and June 7 at the SLA 2005 Annual Conference

NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:11:56 ON 31 MAY 2005

=>
Uploading
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Do you want to switch to the Registry File?
Choice (Y/n):
Switching to the Registry File...
Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	2.52	2.52

FILE 'REGISTRY' ENTERED AT 14:18:54 ON 31 MAY 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 29 MAY 2005 HIGHEST RN 851364-46-0
DICTIONARY FILE UPDATES: 29 MAY 2005 HIGHEST RN 851364-46-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

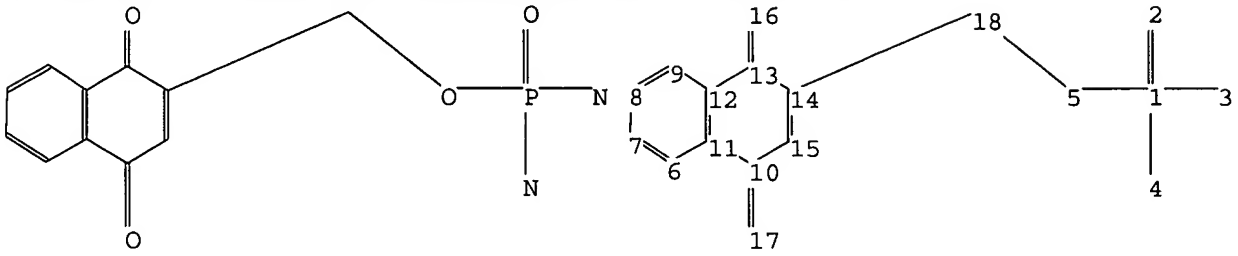
****
*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*
****

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer

to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\10725191.str

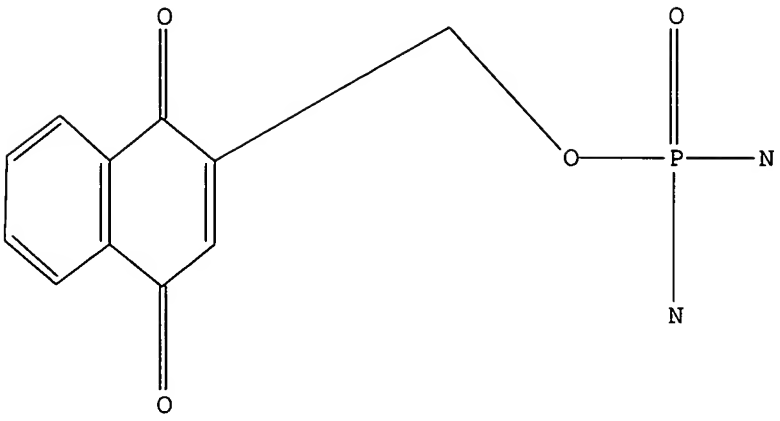


chain nodes :
1 2 3 4 5 16 17 18
ring nodes :
6 7 8 9 10 11 12 13 14 15
chain bonds :
1-2 1-3 1-4 1-5 5-18 10-17 13-16 14-18
ring bonds :
6-7 6-11 7-8 8-9 9-12 10-11 10-15 11-12 12-13 13-14 14-15
exact/norm bonds :
1-2 1-3 1-4 1-5 5-18 10-17 13-16
exact bonds :
10-11 10-15 12-13 13-14 14-15 14-18
normalized bonds :
6-7 6-11 7-8 8-9 9-12 11-12
isolated ring systems :
containing 6 :

Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:Atom 7:Atom 8:Atom 9:Atom
10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:CLASS 17:CLASS 18:CLASS

L1 STRUCTURE UPLOADED

=> D L1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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=> S L1
SAMPLE SEARCH INITIATED 14:19:11 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      0 TO ITERATE

100.0% PROCESSED       0 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.06

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            0 TO        0
PROJECTED ANSWERS:               0 TO        0

L2             0 SEA SSS SAM L1

=> S L1 SSS FULL
FULL SEARCH INITIATED 14:19:24 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     37 TO ITERATE

100.0% PROCESSED      37 ITERATIONS                             10 ANSWERS
SEARCH TIME: 00.00.01

L3            10 SEA SSS FUL L1

=> FIL CAPLUS
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                             161.33     163.85

FILE 'CAPLUS' ENTERED AT 14:19:30 ON 31 MAY 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 31 May 2005 VOL 142 ISS 23
FILE LAST UPDATED: 30 May 2005 (20050530/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L3
L4 2 L3

=> d l4 ibib abs hitstr tot

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:50656 CAPLUS
DOCUMENT NUMBER: 134:95489
TITLE: Phosphoramide compounds, their preparation, pharmaceutical compositions containing them, and their use in the treatment of cancer
INVENTOR(S): Borch, Richard F.; Hernick, Marcy; Flader, Carolee
PATENT ASSIGNEE(S): Purdue Research Foundation, USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001004130	A1	20010118	WO 2000-US19361	20000714
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CU, CZ, DE, DK, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2003008850	A1	20030109	US 2002-47465	20020114
US 6656926	B2	20031202		
US 2004176332	A1	20040909	US 2003-725191	20031201
PRIORITY APPLN. INFO.:			US 1999-143799P	P 19990714
			WO 2000-US19361	A1 20000714
			US 2002-47465	A1 20020114

OTHER SOURCE(S): MARPAT 134:95489
AB The invention provides compds. R1CH2OP(:O)(NRcRd)NRaRb [R1 = organic releasing group comprising quinone ring; Ra-Rd = H, C1-6 alkyl, CH2CH2X; X = halo, C1-6 alkylsulfonyl, halo(C1-6)alkylsulfonyl ((substituted)aryl)sulfonyl; provided that ≥2 of Ra-Rd are CH2CH2X], as well as pharmaceutical compns. comprising such compds. or

salts. The compds. are useful for treating cancer in animals. Preparation of the compds. of the invention is described.

IT **289896-35-1P 289896-38-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(phosphoramide compound preparation, pharmaceutical compns., and use in treatment of cancer)

RN 289896-35-1 CAPLUS
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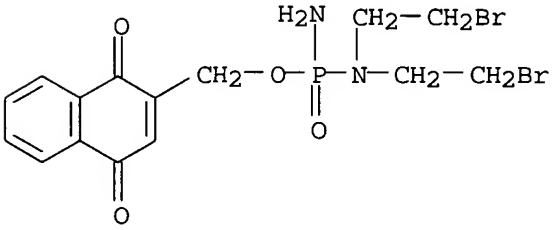

RN 289896-38-4 CAPLUS
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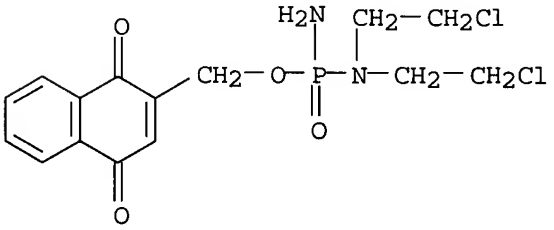
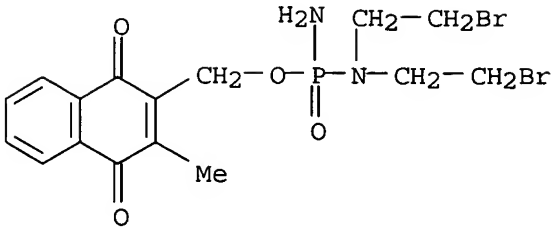
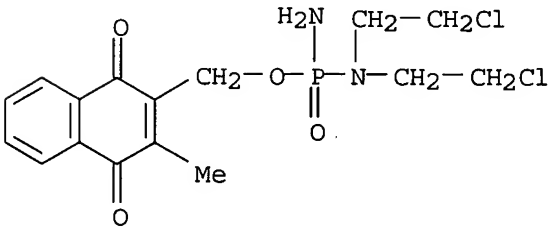


IT **289896-36-2P 289896-46-4P 289896-47-5P**
289896-48-6P 289896-50-0P 289896-58-8P
289896-59-9P 289896-60-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phosphoramide compound preparation, pharmaceutical compns., and use in treatment of cancer)

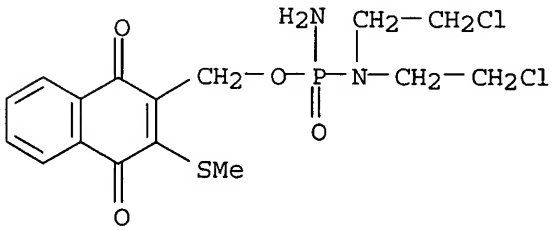
RN 289896-36-2 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-bromoethyl)-, (1,4-dihydro-3-methyl-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



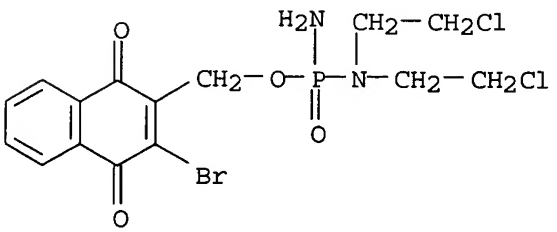
RN 289896-46-4 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (1,4-dihydro-3-methyl-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



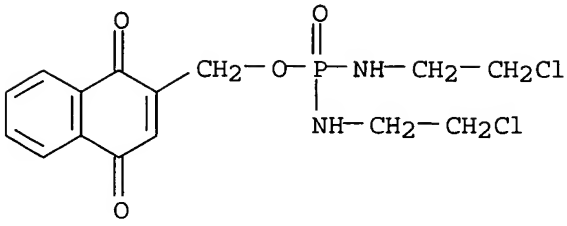
RN 289896-47-5 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, [1,4-dihydro-3-(methylthio)-1,4-dioxo-2-naphthalenyl]methyl ester (9CI) (CA INDEX NAME)



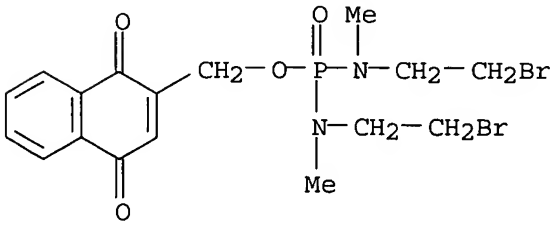
RN 289896-48-6 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (3-bromo-1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



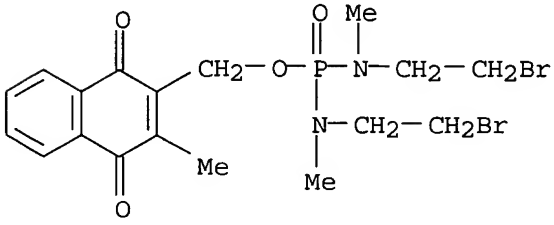
RN 289896-50-0 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-chloroethyl)-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



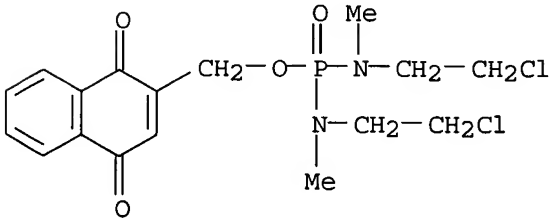
RN 289896-58-8 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-bromoethyl)-N,N'-dimethyl-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



RN 289896-59-9 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-bromoethyl)-N,N'-dimethyl-, (1,4-dihydro-3-methyl-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



RN 289896-60-2 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-chloroethyl)-N,N'-dimethyl-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS

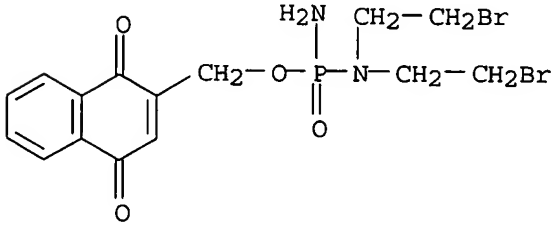
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:481806 CAPLUS
DOCUMENT NUMBER: 133:202587
TITLE: Development of Novel Quinone Phosphorodiamidate Prodrugs Targeted to DT-Diaphorase
AUTHOR(S): Flader, Carolee; Liu, Jiwen; Borch, Richard F.
CORPORATE SOURCE: Departments of Chemistry and Pharmacology, University of Rochester, Rochester, NY, 14642, USA
SOURCE: Journal of Medicinal Chemistry (2000), 43(16), 3157-3167
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of naphthoquinone and benzimidazolequinone phosphorodiamidates has been synthesized and studied as potential cytotoxic prodrugs activated by DT-diaphorase. Reduction of the quinone moiety in the target compds. was expected to provide a pathway for expulsion of the phosphoramide mustard alkylating agent. All of the compds. synthesized were excellent substrates for purified human DT-diaphorase (kcat/Km = 3+107 - 3+108 M-1 s-1). The naphthoquinones were toxic to both HT-29 and BE human colon cancer cell lines in a clonogenic assay; however, cytotoxicity did not correlate with DT-diaphorase activity in these cell lines. The benzimidazolequinone analogs were 1-2 orders of magnitude less cytotoxic than the naphthoquinone analogs. Chemical reduction of the naphthoquinone led to rapid expulsion of the phosphorodiamidate anion; in contrast, the benzimidazole reduction product was stable. Michael addition of glutathione and other sulfur nucleophiles provides an alternate mechanism for activation of the naphthoquinone phosphorodiamidates, and this mechanism may contribute to the cytotoxicity of these compds.

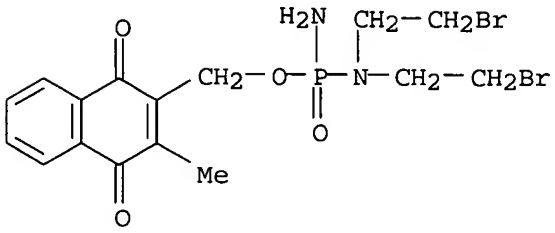
IT **289896-35-1P 289896-36-2P 289896-38-4P**
289896-46-4P 289896-47-5P 289896-48-6P
289896-50-0P 289896-58-8P 289896-59-9P
289896-60-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antitumor structure-activity relations of novel quinone phosphorodiamidate prodrugs targeted to DT-diaphorase)

RN 289896-35-1 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-bromoethyl)-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



RN 289896-36-2 CAPLUS

CN Phosphorodiamidic acid, N,N-bis(2-bromoethyl)-, (1,4-dihydro-3-methyl-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



RN 289896-38-4 CAPLUS
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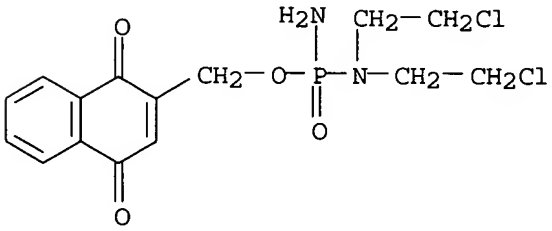

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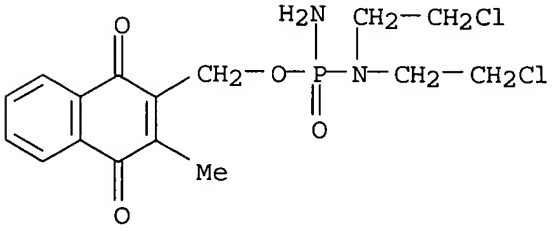
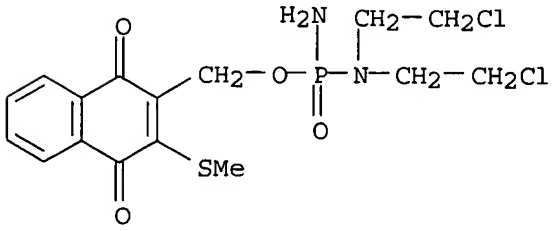
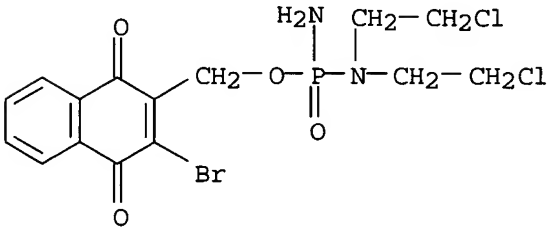


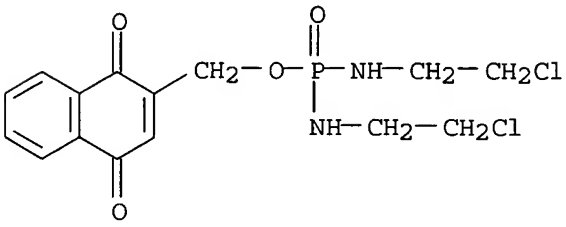
RN 289896-47-5 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, [1,4-dihydro-3-(methylthio)-1,4-dioxo-2-naphthalenyl]methyl ester (9CI) (CA INDEX NAME)



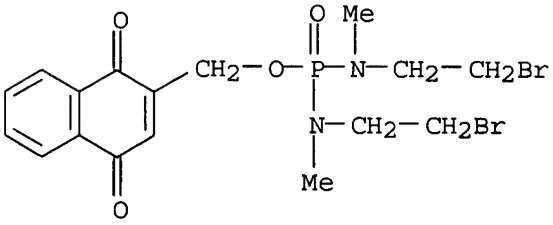
RN 289896-48-6 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (3-bromo-1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



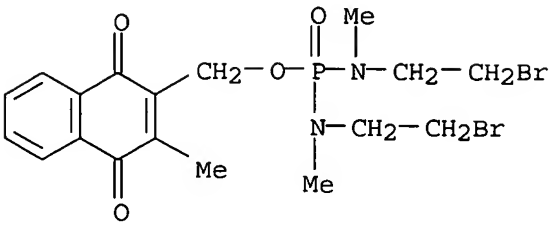
RN 289896-50-0 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-chloroethyl)-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



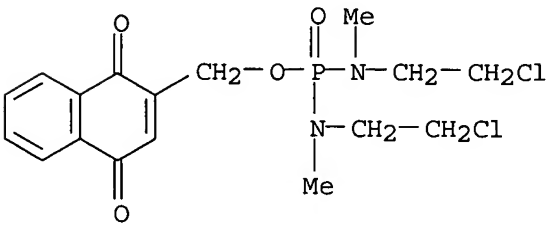
RN 289896-58-8 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-bromoethyl)-N,N'-dimethyl-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



RN 289896-59-9 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-bromoethyl)-N,N'-dimethyl-, (1,4-dihydro-3-methyl-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



RN 289896-60-2 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-chloroethyl)-N,N'-dimethyl-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> FIL REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	11.68	175.53

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.46	-1.46

FILE 'REGISTRY' ENTERED AT 14:21:41 ON 31 MAY 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 29 MAY 2005 HIGHEST RN 851364-46-0
DICTIONARY FILE UPDATES: 29 MAY 2005 HIGHEST RN 851364-46-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

****
*

```
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information.  *
*                                                                    *
**********************************************************************

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\10725191a.str
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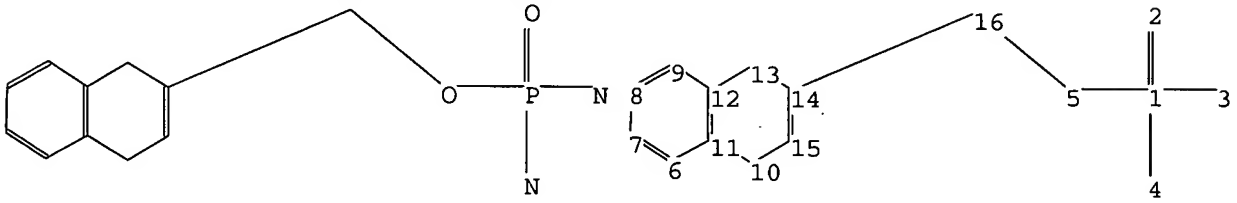


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chain nodes :
1  2  3  4  5  16
ring nodes :
6  7  8  9  10  11  12  13  14  15
chain bonds :
1-2  1-3  1-4  1-5  5-16  14-16
ring bonds :
6-7  6-11  7-8  8-9  9-12  10-11  10-15  11-12  12-13  13-14  14-15
exact/norm bonds :
1-2  1-3  1-4  1-5  5-16
exact bonds :
10-11  10-15  12-13  13-14  14-15  14-16
normalized bonds :
6-7  6-11  7-8  8-9  9-12  11-12
isolated ring systems :
containing 6 :


Match level :
1:CLASS  2:CLASS  3:CLASS  4:CLASS  5:CLASS  6:Atom  7:Atom  8:Atom  9:Atom
10:Atom  11:Atom  12:Atom  13:Atom  14:Atom  15:Atom  16:CLASS



L5      STRUCTURE UPLOADED

=> d l5
L5 HAS NO ANSWERS
L5              STR
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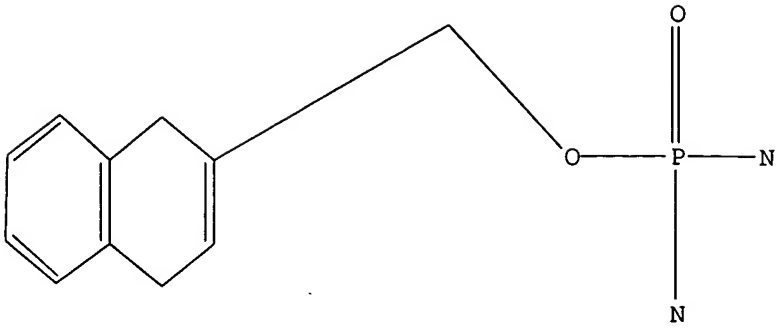

Structure attributes must be viewed using STN Express query preparation.

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=> s l5
SAMPLE SEARCH INITIATED 14:21:58 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      0 TO ITERATE

100.0% PROCESSED      0 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:             0 TO        0
PROJECTED ANSWERS:                0 TO        0

L6            0 SEA SSS SAM L5

=> s l5 sss full
FULL SEARCH INITIATED 14:22:03 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     27 TO ITERATE

100.0% PROCESSED      27 ITERATIONS                              10 ANSWERS
SEARCH TIME: 00.00.01

L7           10 SEA SSS FUL L5

=>
Uploading C:\Program Files\Stnexp\Queries\10725191 b.str
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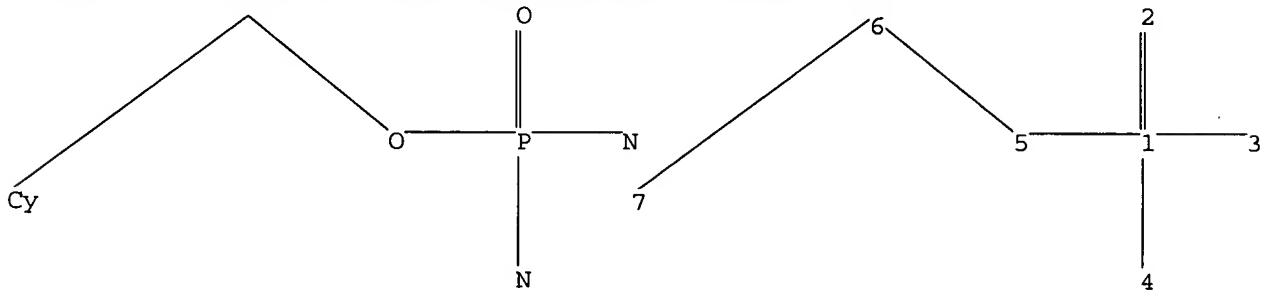


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chain nodes :
1  2  3  4  5  6  7
chain bonds :
1-2  1-3  1-4  1-5  5-6  6-7
```
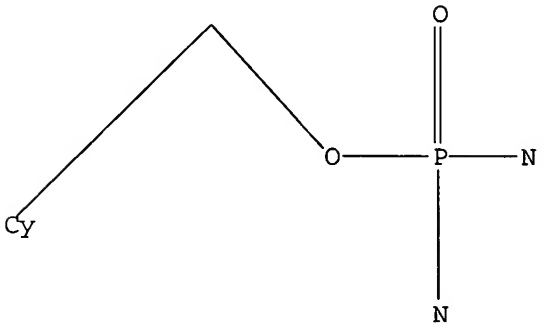

exact/norm bonds :
1-2 1-3 1-4 1-5 5-6 6-7

Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:Atom

L8 STRUCTURE UPLOADED

=> d l8
L8 HAS NO ANSWERS
L8 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l8
SAMPLE SEARCH INITIATED 14:28:45 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 408 TO ITERATE

100.0% PROCESSED 408 ITERATIONS 19 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 6949 TO 9371
PROJECTED ANSWERS: 119 TO 641

L9 19 SEA SSS SAM L8

=> s l8 sss full
FULL SEARCH INITIATED 14:28:51 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 8095 TO ITERATE

100.0% PROCESSED 8095 ITERATIONS 487 ANSWERS
SEARCH TIME: 00.00.01

L10 487 SEA SSS FUL L8

=> FIL CAPLUS
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION

```
FULL ESTIMATED COST                                    326.96      502.49

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)        SINCE FILE       TOTAL
                                                       ENTRY     SESSION
CA SUBSCRIBER PRICE                                     0.00       -1.46

FILE 'CAPLUS' ENTERED AT 14:28:56 ON 31 MAY 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 31 May 2005  VOL 142 ISS 23
FILE LAST UPDATED: 30 May 2005  (20050530/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> d his

     (FILE 'HOME' ENTERED AT 14:11:56 ON 31 MAY 2005)

     FILE 'REGISTRY' ENTERED AT 14:18:54 ON 31 MAY 2005
L1              STRUCTURE UPLOADED
L2            0 S L1
L3           10 S L1 SSS FULL

     FILE 'CAPLUS' ENTERED AT 14:19:30 ON 31 MAY 2005
L4            2 S L3

     FILE 'REGISTRY' ENTERED AT 14:21:41 ON 31 MAY 2005
L5              STRUCTURE UPLOADED
L6            0 S L5
L7           10 S L5 SSS FULL
L8              STRUCTURE UPLOADED
L9           19 S L8
L10         487 S L8 SSS FULL

     FILE 'CAPLUS' ENTERED AT 14:28:56 ON 31 MAY 2005

=> s l7
L11           2 L7

=> s l10
L12         189 L10

=> s l12 and quinone
```

```
          33821 QUINONE
          17757 QUINONES
          42476 QUINONE
                  (QUINONE OR QUINONES)
L13           4 L12 AND QUINONE

=> s l12 and thu
            144 THU
        2238039 THUS
        2238168 THU
                  (THU OR THUS)
L14          34 L12 AND THU

=> s l14 and p/dt
        4708566 P/DT
L15          22 L14 AND P/DT

=> s l15 and py<=1999
       19743743 PY<=1999
L16          19 L15 AND PY<=1999

=> s l16 and us/pc
        1376888 US/PC
L17           7 L16 AND US/PC

=> d his

     (FILE 'HOME' ENTERED AT 14:11:56 ON 31 MAY 2005)

     FILE 'REGISTRY' ENTERED AT 14:18:54 ON 31 MAY 2005
L1               STRUCTURE UPLOADED
L2             0 S L1
L3            10 S L1 SSS FULL

     FILE 'CAPLUS' ENTERED AT 14:19:30 ON 31 MAY 2005
L4             2 S L3

     FILE 'REGISTRY' ENTERED AT 14:21:41 ON 31 MAY 2005
L5               STRUCTURE UPLOADED
L6             0 S L5
L7            10 S L5 SSS FULL
L8               STRUCTURE UPLOADED
L9            19 S L8
L10          487 S L8 SSS FULL

     FILE 'CAPLUS' ENTERED AT 14:28:56 ON 31 MAY 2005
L11            2 S L7
L12          189 S L10
L13            4 S L12 AND QUINONE
L14           34 S L12 AND THU
L15           22 S L14 AND P/DT
L16           19 S L15 AND PY<=1999
L17            7 S L16 AND US/PC

=> d l11 ibib abs hitstr tot

L11  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2001:50656  CAPLUS
DOCUMENT NUMBER:          134:95489
```

TITLE: Phosphoramide compounds, their preparation, pharmaceutical compositions containing them, and their use in the treatment of cancer
INVENTOR(S): Borch, Richard F.; Hernick, Marcy; Flader, Carolee
PATENT ASSIGNEE(S): Purdue Research Foundation, USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001004130	A1	20010118	WO 2000-US19361	20000714
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CU, CZ, DE, DK, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2003008850	A1	20030109	US 2002-47465	20020114
US 6656926	B2	20031202		
US 2004176332	A1	20040909	US 2003-725191	20031201

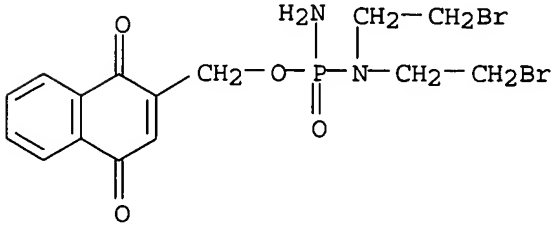
PRIORITY APPLN. INFO.:
US 1999-143799P P 19990714
WO 2000-US19361 A1 20000714
US 2002-47465 A1 20020114

OTHER SOURCE(S): MARPAT 134:95489

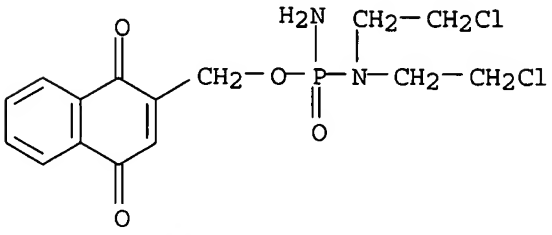
AB The invention provides compds. R1CH2OP(:O)(NRcRd)NRaRb [R1 = organic releasing group comprising quinone ring; Ra-Rd = H, C1-6 alkyl, CH2CH2X; X = halo, C1-6 alkylsulfonyl, halo(C1-6)alkylsulfonyl ((substituted)aryl)sulfonyl; provided that ≥2 of Ra-Rd are CH2CH2X], as well as pharmaceutical compns. comprising such compds. or salts. The compds. are useful for treating cancer in animals. Preparation of the compds. of the invention is described.

IT **289896-35-1P 289896-38-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(phosphoramide compound preparation, pharmaceutical compns., and use in treatment of cancer)

RN 289896-35-1 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-bromoethyl)-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)

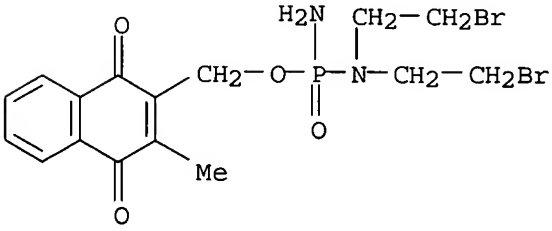


RN 289896-38-4 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)

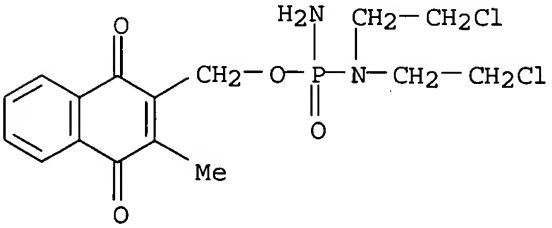


IT **289896-36-2P 289896-46-4P 289896-47-5P**
289896-48-6P 289896-50-0P 289896-58-8P
289896-59-9P 289896-60-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phosphoramide compound preparation, pharmaceutical compns., and use in treatment of cancer)

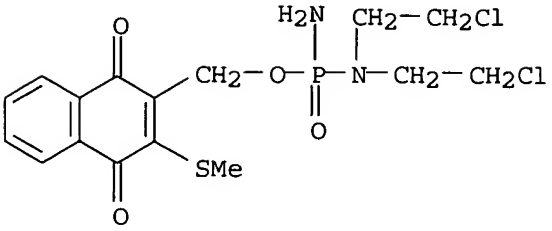
RN 289896-36-2 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-bromoethyl)-, (1,4-dihydro-3-methyl-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



RN 289896-46-4 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (1,4-dihydro-3-methyl-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



RN 289896-47-5 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, [1,4-dihydro-3-(methylthio)-1,4-dioxo-2-naphthalenyl]methyl ester (9CI) (CA INDEX NAME)



RN 289896-48-6 CAPLUS
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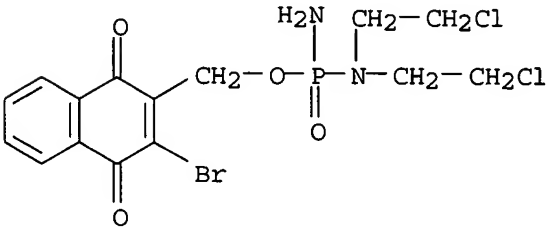

RN 289896-50-0 CAPLUS
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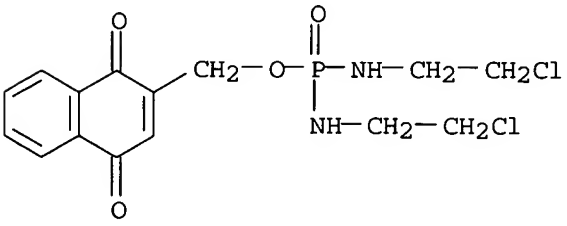
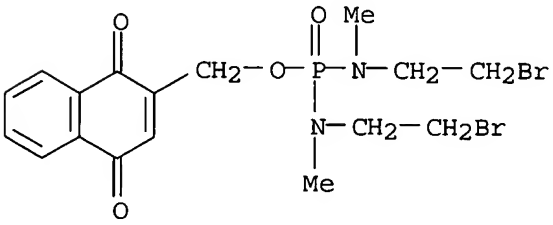
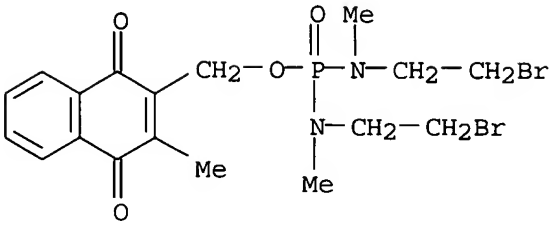


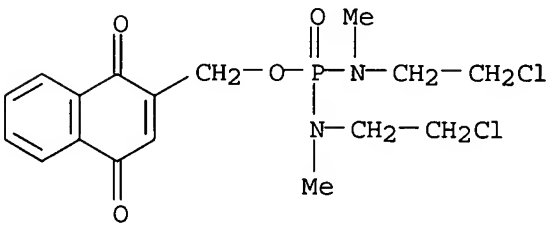
RN 289896-58-8 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-bromoethyl)-N,N'-dimethyl-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



RN 289896-59-9 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-bromoethyl)-N,N'-dimethyl-, (1,4-dihydro-3-methyl-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



RN 289896-60-2 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-chloroethyl)-N,N'-dimethyl-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

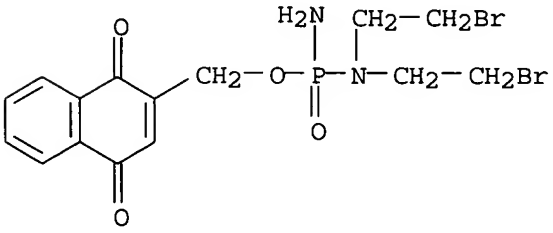
L11 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:481806 CAPLUS
DOCUMENT NUMBER: 133:202587
TITLE: Development of Novel Quinone Phosphorodiamidate Prodrugs Targeted to DT-Diaphorase
AUTHOR(S): Flader, Carolee; Liu, Jiwen; Borch, Richard F.
CORPORATE SOURCE: Departments of Chemistry and Pharmacology, University of Rochester, Rochester, NY, 14642, USA
SOURCE: Journal of Medicinal Chemistry (2000), 43(16), 3157-3167
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of naphthoquinone and benzimidazolequinone phosphorodiamidates has been synthesized and studied as potential cytotoxic prodrugs activated by DT-diaphorase. Reduction of the quinone moiety in the target compds. was expected to provide a pathway for expulsion of the phosphoramide mustard alkylating agent. All of the compds. synthesized were excellent substrates for purified human DT-diaphorase (kcat/Km = 3+107 - 3+108 M-1 s-1). The naphthoquinones were toxic to both HT-29 and BE human colon cancer cell lines in a clonogenic assay; however, cytotoxicity did not correlate with DT-diaphorase activity in these cell lines. The benzimidazolequinone analogs were 1-2 orders of magnitude less cytotoxic than the naphthoquinone analogs. Chemical reduction of the naphthoquinone led to rapid expulsion of the phosphorodiamidate anion; in contrast, the benzimidazole reduction product was stable. Michael addition of glutathione and

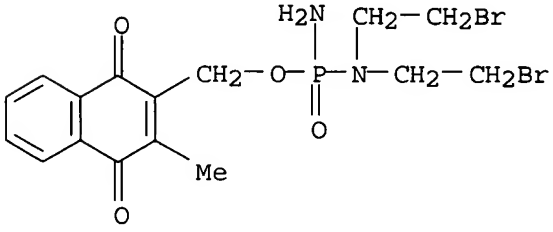
other sulfur nucleophiles provides an alternate mechanism for activation of the naphthoquinone phosphorodiamidates, and this mechanism may contribute to the cytotoxicity of these compds.

IT **289896-35-1P 289896-36-2P 289896-38-4P**
289896-46-4P 289896-47-5P 289896-48-6P
289896-50-0P 289896-58-8P 289896-59-9P
289896-60-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antitumor structure-activity relations of novel quinone phosphorodiamidate prodrugs targeted to DT-diaphorase)

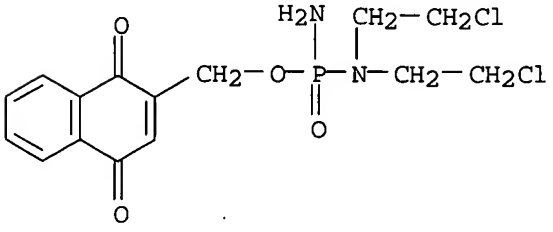
RN 289896-35-1 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-bromoethyl)-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



RN 289896-36-2 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-bromoethyl)-, (1,4-dihydro-3-methyl-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)

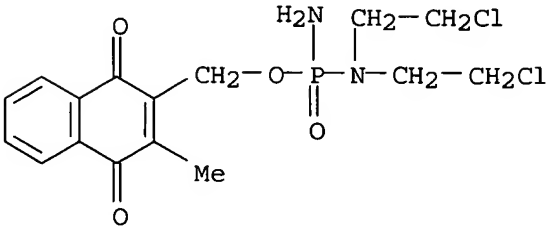


RN 289896-38-4 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)

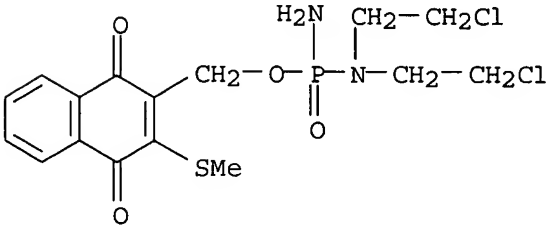


RN 289896-46-4 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (1,4-dihydro-3-methyl-1,4-

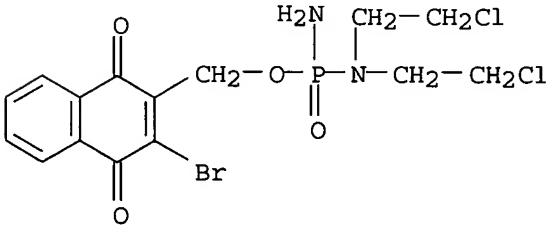
dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



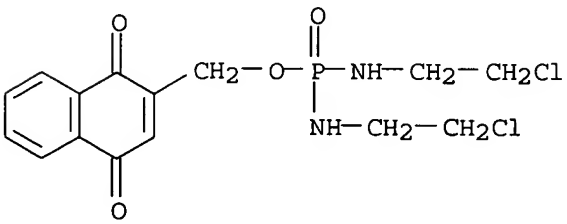
RN 289896-47-5 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, [1,4-dihydro-3-(methylthio)-1,4-dioxo-2-naphthalenyl]methyl ester (9CI) (CA INDEX NAME)



RN 289896-48-6 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (3-bromo-1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)

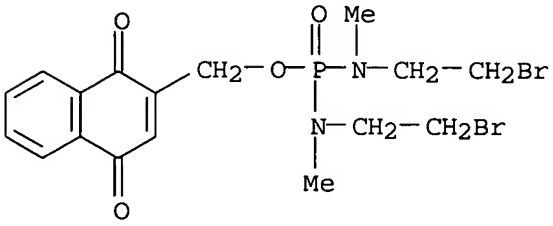


RN 289896-50-0 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-chloroethyl)-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)

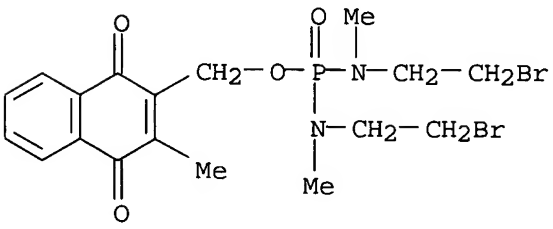


RN 289896-58-8 CAPLUS

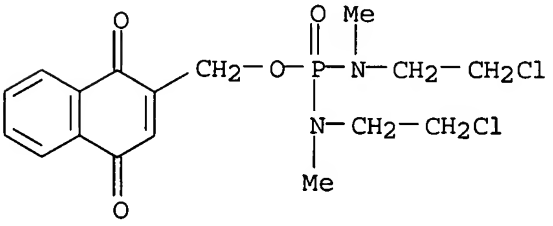
CN Phosphorodiamidic acid, N,N'-bis(2-bromoethyl)-N,N'-dimethyl-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



RN 289896-59-9 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-bromoethyl)-N,N'-dimethyl-, (1,4-dihydro-3-methyl-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



RN 289896-60-2 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-chloroethyl)-N,N'-dimethyl-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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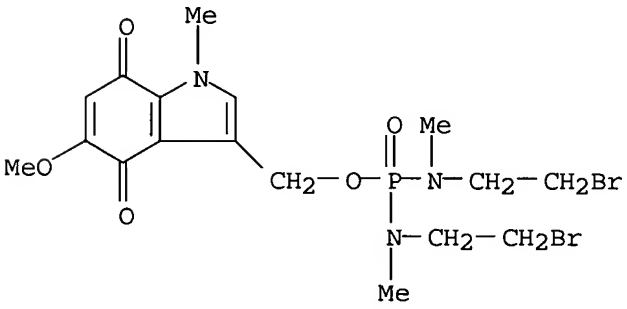
L13 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:509532 CAPLUS
DOCUMENT NUMBER: 137:201392
TITLE: Design, Synthesis, and Biological Evaluation of Indolequinone Phosphoramidate Prodrugs Targeted to DT-diaphorase
AUTHOR(S): Hernick, Marcy; Flader, Carolee; Borch, Richard F.
CORPORATE SOURCE: Department of Medicinal Chemistry and Molecular

Pharmacology and the Cancer Center, Purdue University, West Lafayette, IN, 47907, USA
SOURCE: Journal of Medicinal Chemistry (2002), 45(16), 3540-3548
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:201392

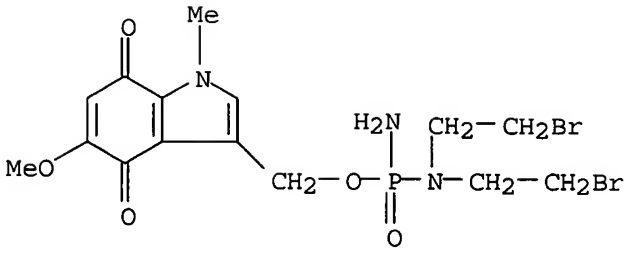
AB 2- And 3-substituted indolequinone phosphoramidate prodrugs targeted to DT-diaphorase (DTD) were synthesized and evaluated. These compds. (e.g. (5-methoxy-1-methyl-4,7-indolequinon-2-yl)methyl N,N-bis(2-bromoethyl)phosphorodiamidate) are designed to undergo activation via **quinone** reduction by DTD followed by expulsion of the phosphoramide mustard substituent from the hydroquinone. Chemical reduction of the phosphoramidate prodrugs led to rapid expulsion of the corresponding phosphoramidate anions in both series of compds. Compds. substituted at the 2-position are excellent substrates for human DTD (kcat/KM = (2-5) + 106 M-1 s-1); however, compds. substituted at the 3-position are potent inhibitors of the target enzyme. Both series of compds. are toxic in HT-29 and BE human colon cancer cell lines in a clonogenic assay. There was a correlation found between cytotoxicity and DTD activity for the 2-series of phosphoramidates; however, there was no correlation between cytotoxicity and DTD activity in the 3-series of compds. This finding suggests an alternative mechanism for the activation of these compds.

IT **318974-70-8P 318974-71-9P 318974-73-1P**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and evaluation of indolequinone phosphoramidates as prodrug targeted to DT-diaphorase)

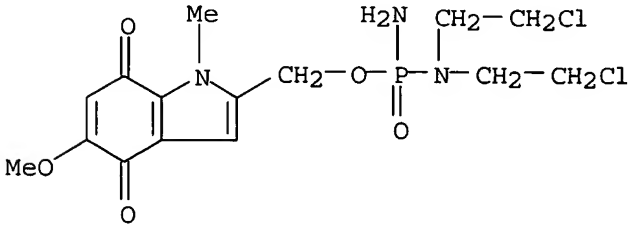
RN 318974-70-8 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-bromoethyl)-N,N'-dimethyl-, (4,7-dihydro-5-methoxy-1-methyl-4,7-dioxo-1H-indol-3-yl)methyl ester (9CI) (CA INDEX NAME)



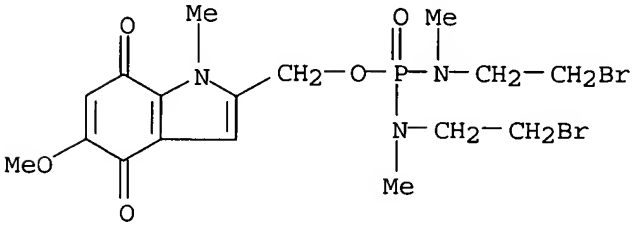
RN 318974-71-9 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-bromoethyl)-, (4,7-dihydro-5-methoxy-1-methyl-4,7-dioxo-1H-indol-3-yl)methyl ester (9CI) (CA INDEX NAME)



RN 318974-73-1 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (4,7-dihydro-5-methoxy-1-methyl-4,7-dioxo-1H-indol-2-yl)methyl ester (9CI) (CA INDEX NAME)

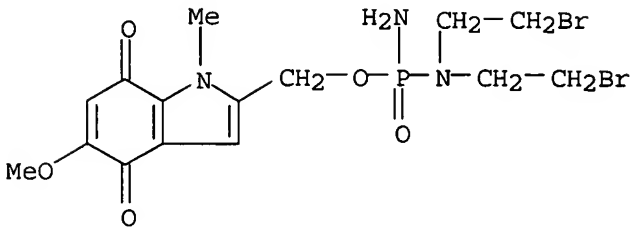


IT **318974-72-0P**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and evaluation of indolequinone phosphoramidates as prodrug targeted to DT-diaphorase)
RN 318974-72-0 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-bromoethyl)-N,N'-dimethyl-, (4,7-dihydro-5-methoxy-1-methyl-4,7-dioxo-1H-indol-2-yl)methyl ester (9CI) (CA INDEX NAME)



IT **318974-74-2P**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation, chemical reduction and evaluation of indolequinone phosphoramidates
as prodrug targeted to DT-diaphorase)
RN 318974-74-2 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-bromoethyl)-, (4,7-dihydro-5-methoxy-1-

methyl-4,7-dioxo-1H-indol-2-yl)methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:50656 CAPLUS
DOCUMENT NUMBER: 134:95489
TITLE: Phosphoramide compounds, their preparation, pharmaceutical compositions containing them, and their use in the treatment of cancer
INVENTOR(S): Borch, Richard F.; Hernick, Marcy; Flader, Carolee
PATENT ASSIGNEE(S): Purdue Research Foundation, USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001004130	A1	20010118	WO 2000-US19361	20000714
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CU, CZ, DE, DK, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2003008850	A1	20030109	US 2002-47465	20020114
US 6656926	B2	20031202		
US 2004176332	A1	20040909	US 2003-725191	20031201
PRIORITY APPLN. INFO.:			US 1999-143799P	P 19990714
			WO 2000-US19361	A1 20000714
			US 2002-47465	A1 20020114

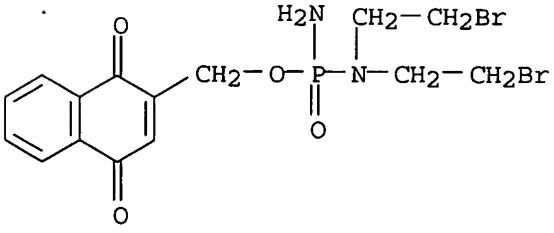
OTHER SOURCE(S): MARPAT 134:95489

AB The invention provides compds. R1CH2OP(:O)(NRcRd)NRaRb [R1 = organic releasing group comprising **quinone** ring; Ra-Rd = H, C1-6 alkyl, CH2CH2X; X = halo, C1-6 alkylsulfonyl, halo(C1-6)alkylsulfonyl ((substituted)aryl)sulfonyl; provided that ≥2 of Ra-Rd are CH2CH2X], as well as pharmaceutical compns. comprising such compds. or salts. The compds. are useful for treating cancer in animals. Preparation of the compds. of the invention is described.

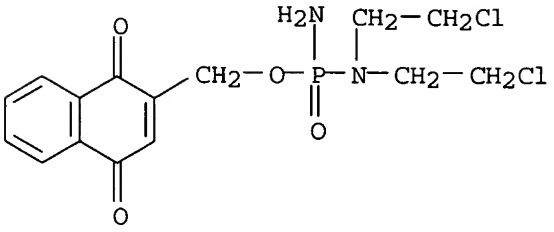
IT **289896-35-1P 289896-38-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(phosphoramide compound preparation, pharmaceutical compns., and use in treatment of cancer)

RN 289896-35-1 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-bromoethyl)-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)

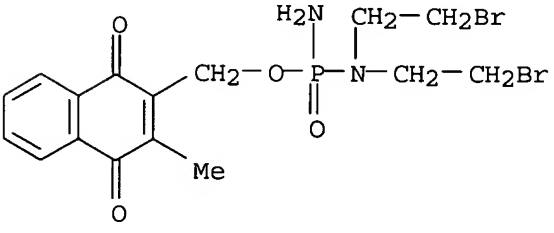


RN 289896-38-4 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)

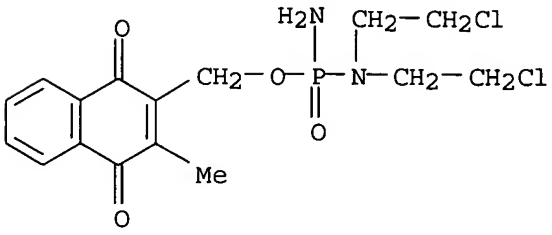


IT **289896-36-2P 289896-46-4P 289896-47-5P**
289896-48-6P 289896-50-0P 289896-58-8P
289896-59-9P 289896-60-2P 318974-70-8P
318974-71-9P 318974-72-0P 318974-73-1P
318974-74-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phosphoramide compound preparation, pharmaceutical compns., and use in treatment of cancer)

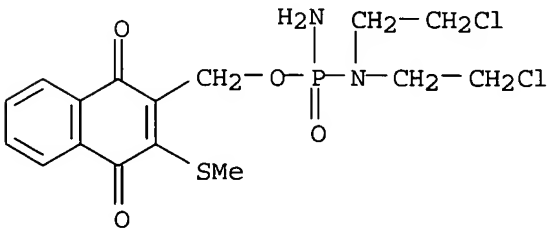
RN 289896-36-2 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-bromoethyl)-, (1,4-dihydro-3-methyl-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



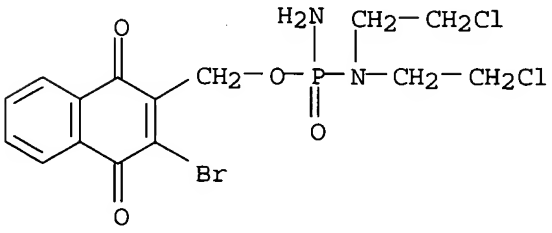
RN 289896-46-4 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (1,4-dihydro-3-methyl-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



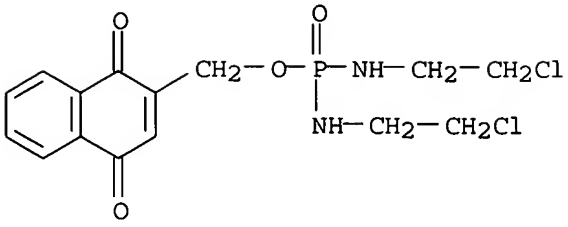
RN 289896-47-5 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, [1,4-dihydro-3-(methylthio)-1,4-dioxo-2-naphthalenyl]methyl ester (9CI) (CA INDEX NAME)



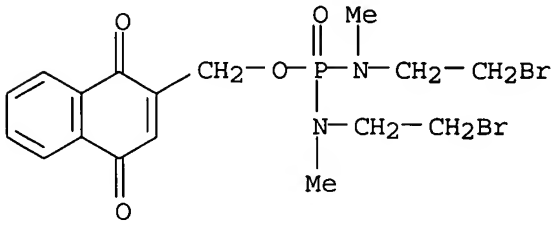
RN 289896-48-6 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (3-bromo-1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



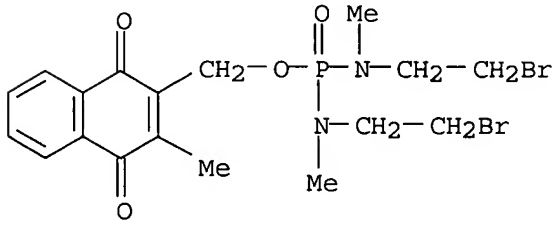
RN 289896-50-0 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-chloroethyl)-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



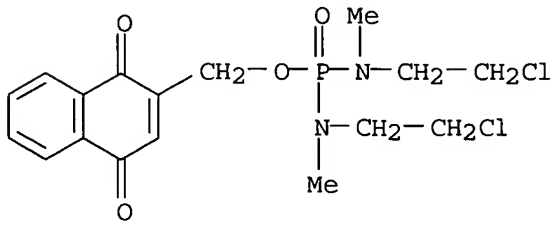
RN 289896-58-8 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-bromoethyl)-N,N'-dimethyl-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



RN 289896-59-9 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-bromoethyl)-N,N'-dimethyl-, (1,4-dihydro-3-methyl-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)

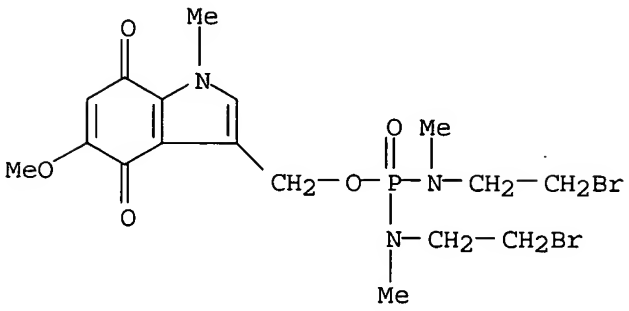


RN 289896-60-2 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-chloroethyl)-N,N'-dimethyl-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)

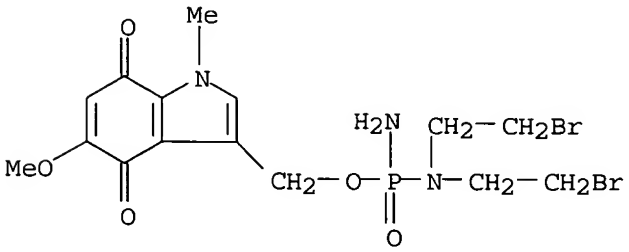


RN 318974-70-8 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-bromoethyl)-N,N'-dimethyl-,

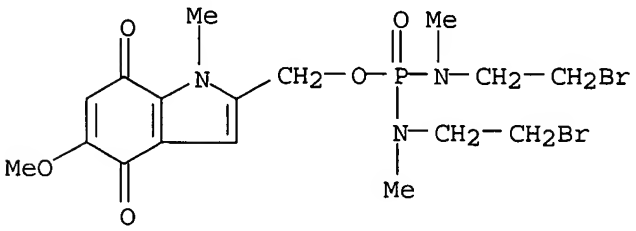
(4,7-dihydro-5-methoxy-1-methyl-4,7-dioxo-1H-indol-3-yl)methyl ester (9CI) (CA INDEX NAME)



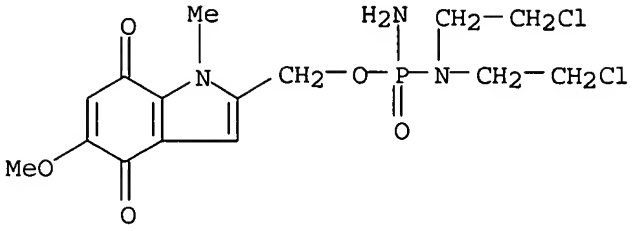
RN 318974-71-9 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-bromoethyl)-, (4,7-dihydro-5-methoxy-1-methyl-4,7-dioxo-1H-indol-3-yl)methyl ester (9CI) (CA INDEX NAME)



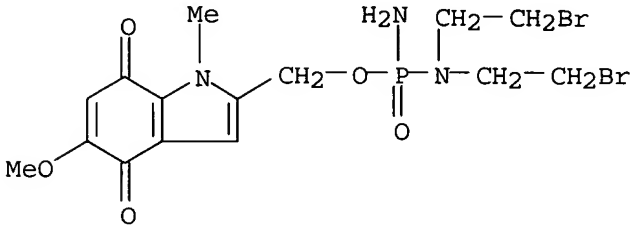
RN 318974-72-0 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-bromoethyl)-N,N'-dimethyl-, (4,7-dihydro-5-methoxy-1-methyl-4,7-dioxo-1H-indol-2-yl)methyl ester (9CI) (CA INDEX NAME)



RN 318974-73-1 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (4,7-dihydro-5-methoxy-1-methyl-4,7-dioxo-1H-indol-2-yl)methyl ester (9CI) (CA INDEX NAME)

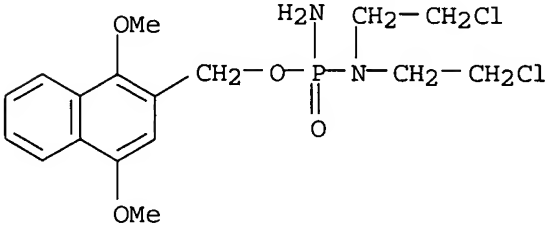


RN 318974-74-2 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-bromoethyl)-, (4,7-dihydro-5-methoxy-1-methyl-4,7-dioxo-1H-indol-2-yl)methyl ester (9CI) (CA INDEX NAME)

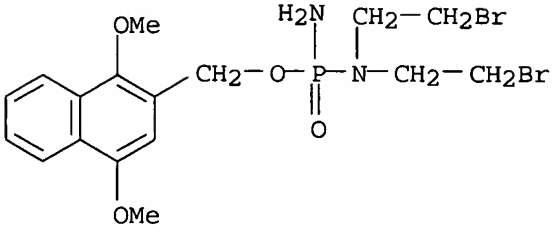


IT **289896-37-3P 289896-41-9P 289896-42-0P**
289896-43-1P 289896-44-2P 289896-45-3P
289896-49-7P 289896-55-5P 289896-56-6P
318974-75-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction; phosphoramide compound preparation, pharmaceutical
compns., and use in treatment of cancer)

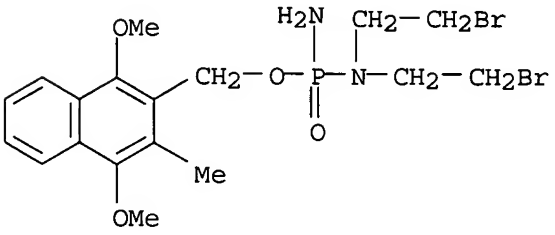
RN 289896-37-3 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (1,4-dimethoxy-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



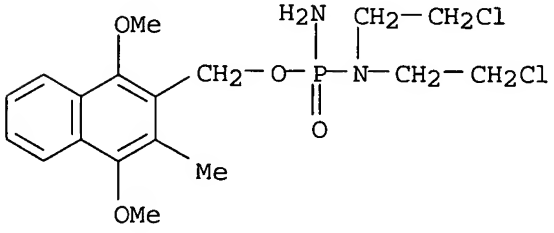
RN 289896-41-9 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-bromoethyl)-, (1,4-dimethoxy-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



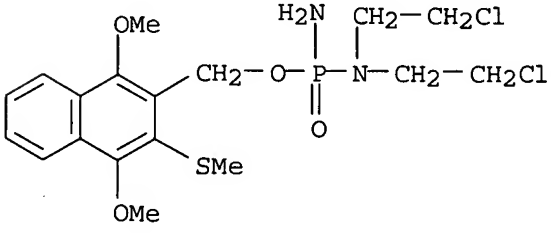
RN 289896-42-0 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-bromoethyl)-, (1,4-dimethoxy-3-methyl-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



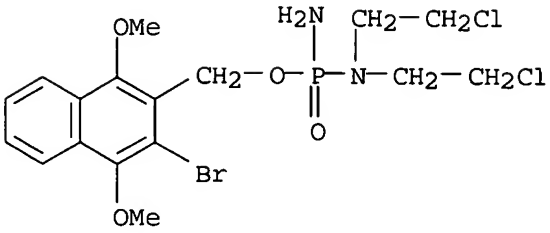
RN 289896-43-1 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (1,4-dimethoxy-3-methyl-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



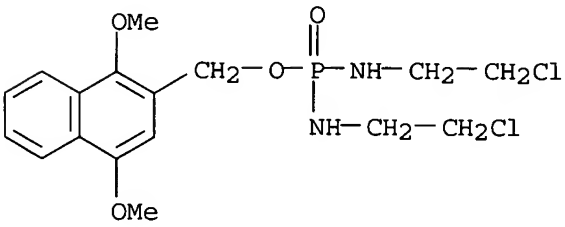
RN 289896-44-2 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, [1,4-dimethoxy-3-(methylthio)-2-naphthalenyl]methyl ester (9CI) (CA INDEX NAME)



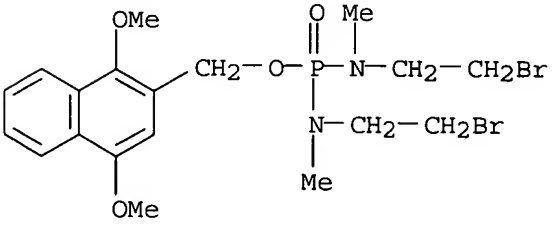
RN 289896-45-3 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (3-bromo-1,4-dimethoxy-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



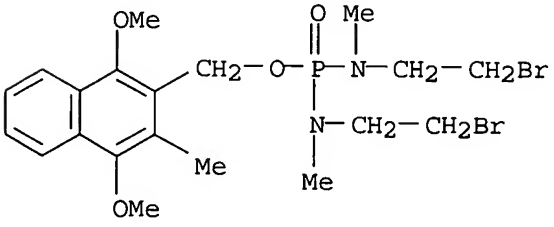
RN 289896-49-7 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-chloroethyl)-, (1,4-dimethoxy-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



RN 289896-55-5 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-bromoethyl)-N,N'-dimethyl-, (1,4-dimethoxy-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)

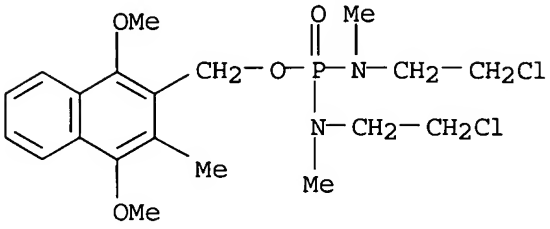


RN 289896-56-6 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-bromoethyl)-N,N'-dimethyl-, (1,4-dimethoxy-3-methyl-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



RN 318974-75-3 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-chloroethyl)-N,N'-dimethyl-,

(1,4-dimethoxy-3-methyl-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

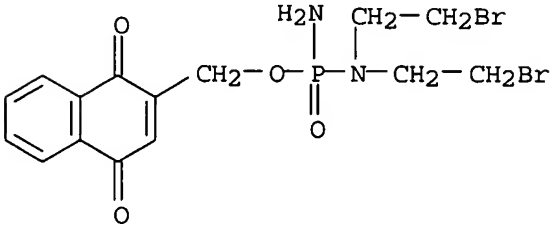
L13 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:481806 CAPLUS
DOCUMENT NUMBER: 133:202587
TITLE: Development of Novel **Quinone** Phosphorodiamidate Prodrugs Targeted to DT-Diaphorase
AUTHOR(S): Flader, Carolee; Liu, Jiwen; Borch, Richard F.
CORPORATE SOURCE: Departments of Chemistry and Pharmacology, University of Rochester, Rochester, NY, 14642, USA
SOURCE: Journal of Medicinal Chemistry (2000), 43(16), 3157-3167
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of naphthoquinone and benzimidazolequinone phosphorodiamidates has been synthesized and studied as potential cytotoxic prodrugs activated by DT-diaphorase. Reduction of the **quinone** moiety in the target compds. was expected to provide a pathway for expulsion of the phosphoramide mustard alkylating agent. All of the compds. synthesized were excellent substrates for purified human DT-diaphorase (kcat/Km = 3+107 - 3+108 M-1 s-1). The naphthoquinones were toxic to both HT-29 and BE human colon cancer cell lines in a clonogenic assay; however, cytotoxicity did not correlate with DT-diaphorase activity in these cell lines. The benzimidazolequinone analogs were 1-2 orders of magnitude less cytotoxic than the naphthoquinone analogs. Chemical reduction of the naphthoquinone led to rapid expulsion of the phosphorodiamidate anion; in contrast, the benzimidazole reduction product was stable. Michael addition of glutathione and other sulfur nucleophiles provides an alternate mechanism for activation of the naphthoquinone phosphorodiamidates, and this mechanism may contribute to the cytotoxicity of these compds.

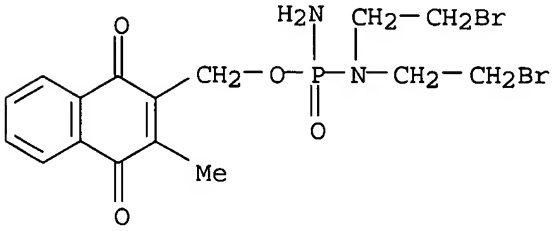
IT **289896-35-1P 289896-36-2P 289896-38-4P**
289896-46-4P 289896-47-5P 289896-48-6P
289896-50-0P 289896-53-3P 289896-54-4P
289896-58-8P 289896-59-9P 289896-60-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antitumor structure-activity relations of novel **quinone** phosphorodiamidate prodrugs targeted to DT-diaphorase)

RN 289896-35-1 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-bromoethyl)-, (1,4-dihydro-1,4-dioxo-2-

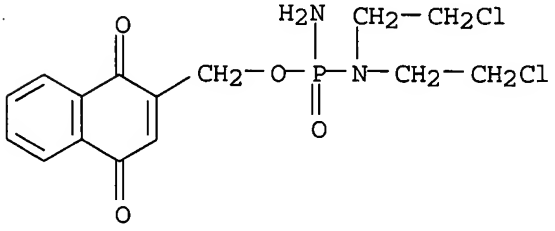
naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



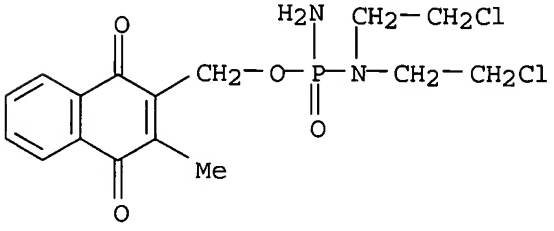
RN 289896-36-2 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-bromoethyl)-, (1,4-dihydro-3-methyl-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



RN 289896-38-4 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)

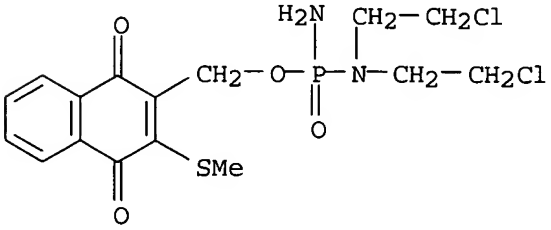


RN 289896-46-4 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (1,4-dihydro-3-methyl-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)

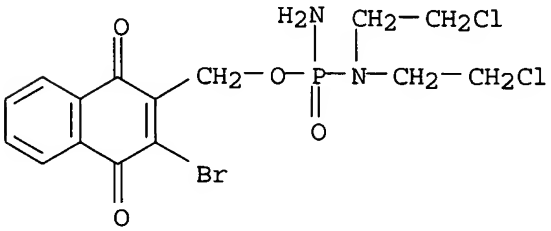


RN 289896-47-5 CAPLUS

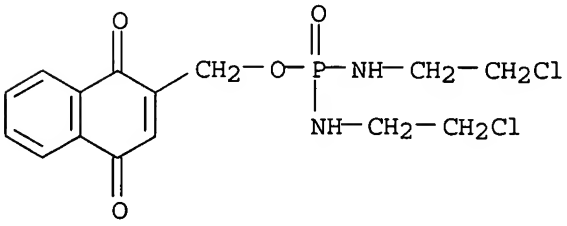
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, [1,4-dihydro-3-(methylthio)-1,4-dioxo-2-naphthalenyl]methyl ester (9CI) (CA INDEX NAME)



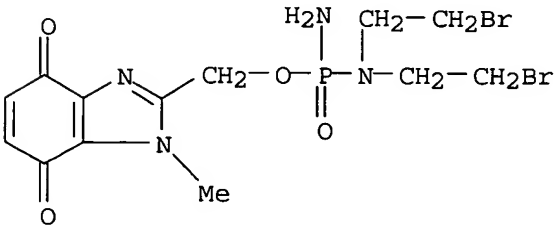
RN 289896-48-6 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (3-bromo-1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



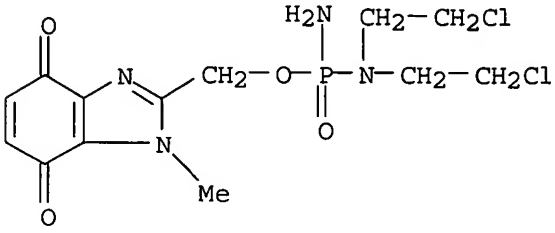
RN 289896-50-0 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-chloroethyl)-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



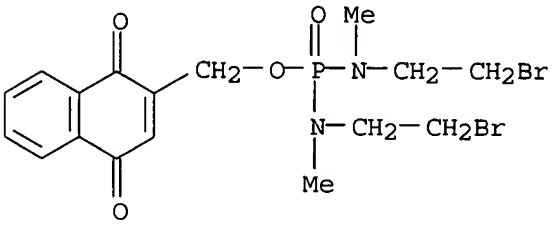
RN 289896-53-3 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-bromoethyl)-, (4,7-dihydro-1-methyl-4,7-dioxo-1H-benzimidazol-2-yl)methyl ester (9CI) (CA INDEX NAME)



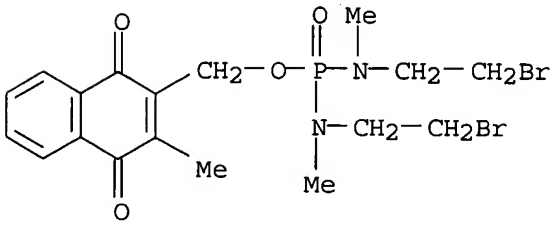
RN 289896-54-4 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (4,7-dihydro-1-methyl-4,7-dioxo-1H-benzimidazol-2-yl)methyl ester (9CI) (CA INDEX NAME)



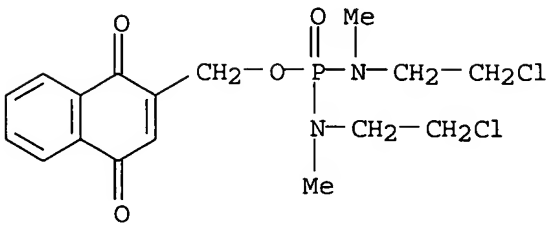
RN 289896-58-8 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-bromoethyl)-N,N'-dimethyl-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



RN 289896-59-9 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-bromoethyl)-N,N'-dimethyl-, (1,4-dihydro-3-methyl-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)

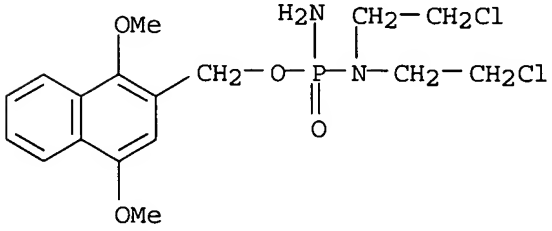


RN 289896-60-2 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-chloroethyl)-N,N'-dimethyl-, (1,4-dihydro-1,4-dioxo-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)

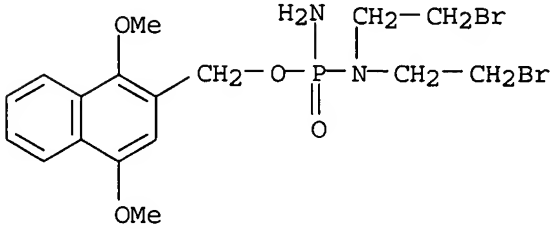


IT **289896-37-3P 289896-41-9P 289896-42-0P**
289896-43-1P 289896-44-2P 289896-45-3P
289896-49-7P 289896-51-1P 289896-52-2P
289896-55-5P 289896-56-6P 289896-57-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antitumor structure-activity relations of novel **quinone** phosphorodiamidate prodrugs targeted to DT-diaphorase)

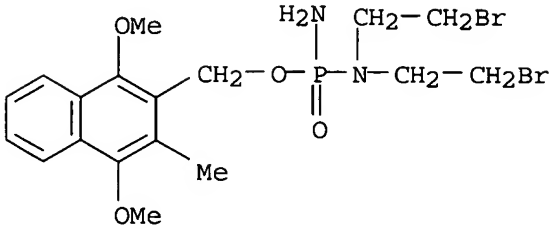
RN 289896-37-3 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (1,4-dimethoxy-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



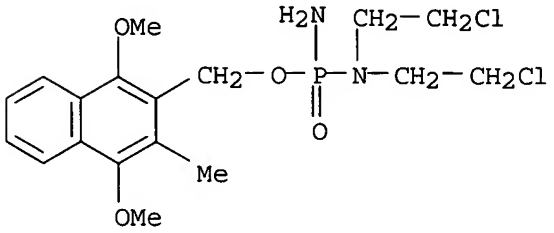
RN 289896-41-9 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-bromoethyl)-, (1,4-dimethoxy-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



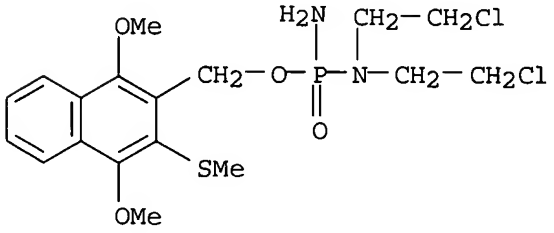
RN 289896-42-0 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-bromoethyl)-, (1,4-dimethoxy-3-methyl-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



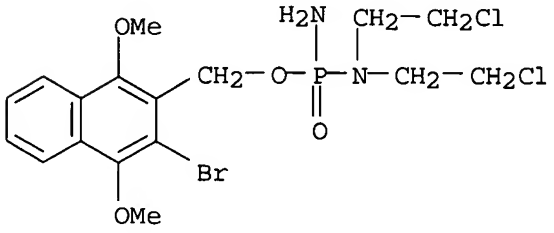
RN 289896-43-1 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (1,4-dimethoxy-3-methyl-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



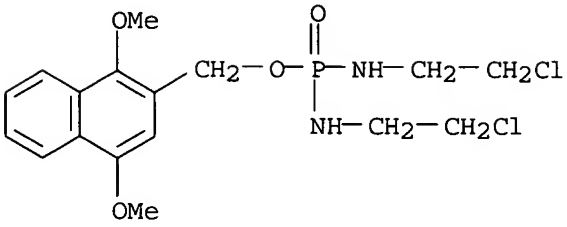
RN 289896-44-2 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, [1,4-dimethoxy-3-(methylthio)-2-naphthalenyl]methyl ester (9CI) (CA INDEX NAME)



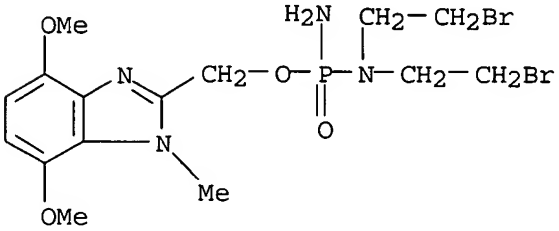
RN 289896-45-3 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (3-bromo-1,4-dimethoxy-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



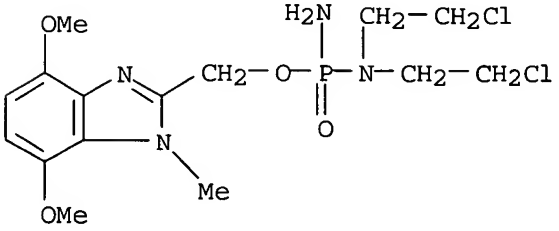
RN 289896-49-7 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-chloroethyl)-, (1,4-dimethoxy-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



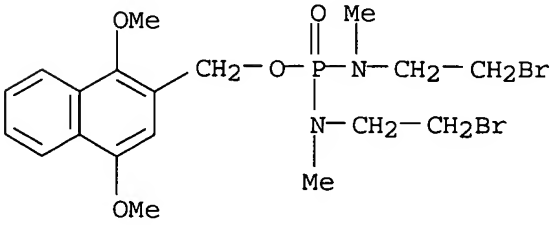
RN 289896-51-1 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-bromoethyl)-, (4,7-dimethoxy-1-methyl-1H-benzimidazol-2-yl)methyl ester (9CI) (CA INDEX NAME)



RN 289896-52-2 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (4,7-dimethoxy-1-methyl-1H-benzimidazol-2-yl)methyl ester (9CI) (CA INDEX NAME)

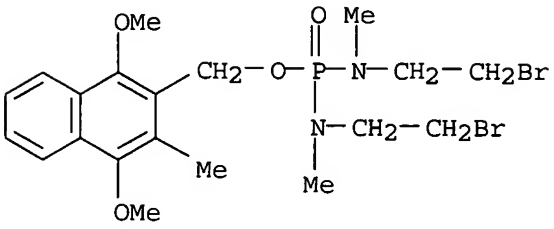


RN 289896-55-5 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-bromoethyl)-N,N'-dimethyl-, (1,4-dimethoxy-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)

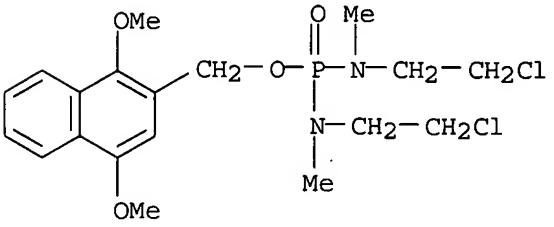


RN 289896-56-6 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-bromoethyl)-N,N'-dimethyl-,

(1,4-dimethoxy-3-methyl-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



RN 289896-57-7 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-chloroethyl)-N,N'-dimethyl-, (1,4-dimethoxy-2-naphthalenyl)methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1962:79428 CAPLUS
DOCUMENT NUMBER: 56:79428
ORIGINAL REFERENCE NO.: 56:15507a-f
TITLE: Phosphorylated pyrimidines
AUTHOR(S): Hodan, James J.; Tieckelmann, Howard
CORPORATE SOURCE: Univ. of Buffalo, Buffalo, NY
SOURCE: Journal of Organic Chemistry (1961), 26, 4429-33
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

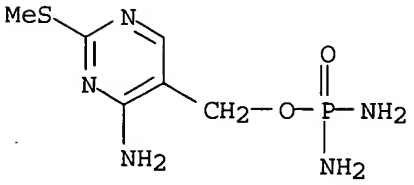
AB A solution of 2.0 g. 4-amino-5-formyl-2-(methylthio)pyrimidine (I), 0.20 g. triethylamine, and 2.6 g. dimethyl hydrogen phosphite in 40 ml. dry MeOH was refluxed 10 hrs. After removal of the solvent and removal of unchanged I the residue was recrystd. from EtOH- Et2O to give 1.12 g. dimethyl 5-[4-amino-2-(methylthio)pyrimidyl]hydroxymethylphosphonate, m. 109-12°. In a similar manner the following compds. were prepared: diethyl 5-[4-amino-2-(methylthio)pyrimidyl]hydroxymethylphosphonate, m. 120-2°; dibutyl 5-[4-amino-2-(methylthio)pyrimidyl]hydroxymethylpho sphonate, m. 171-3° (decomposition); diphenyl 5-[4-amino-2-(methylthio)pyrimidyl]hydroxymethylphosphonate, m. 134-6°, diethyl 5-(4-amino-2-hydroxypyrimidyl)hydroxymethylphosphonate hydrochloride, m. 88-91°; 5-(4-amino-2-hydroxypyrimidyl)hydroxymethylphosphonic acid, m. 300-3° (decomposition); diethyl 5-[4-amino-5-(methylsulfonyl)pyrimidyl]hydroxymethylphosphonate, m. 181-3°; and diethyl 5-(2,4-diaminopyrimidyl)hydroxymethylphosphonate, m. above 220° (decomposition). 5-[4-Amino-2-(methylthio)pyrimidyl] methylphosphonates were prepared by heating 0.012 mole trialkyl phosphite

and 4-amino-5-bromomethyl-2-(methylthio)pyrimidine hydrobromide at 100-180° 4-6 hrs. The amber solid, which formed on cooling was purified by recrystn. from ethanol-ether and ethanol-acetone, and methanolacetone. The following 5-(4-amino-2-(methylthio)pyrimidyl)methyl phosphonates were prepared (alkyl substituent, % yield, m.p. given): Me, 52, 281-4° (decomposition); Et, 52, 268-70° (decomposition), iso-Pr, 47, 286-9 ° (decomposition), C6H13, 47, 121-3°, Ph, 43, 197-200° (decomposition). The reaction of POCl3 with 2-(methylthio)-4-amino-5-hydroxymethylpyrimidine (II) gave 5-(4-amino-2-(methylthio)pyrimidyl)methyl phosphorodichloridate (III), m. 260° (decomposition). III and ethylenimine gave 5-(4-amino-2-methylthiopyrimidyl)methyl N,N-diethylenephosphorodiamidate, m. 176-9° (decomposition), thiophosphoryl chloride and II gave 5-(4-amino-2-methylthiopyrimidyl)methyl phosphorodichlorothioate, m. 231-4° (decomposition). This was used as an intermediate to form 5-(4-amino-2-methylthiopyrimidyl)methyl N,N'-diethylenephosphorodiamidothioate, m. 193-6°. Diethyl and dimethyl thionochlorophosphate treated with II in the presence of triethylamine gave diethyl and dimethyl 5-(4-amino-2-methylthiopyrimidyl)methyl phosphorothioate hydrochloride, m. 157-9° (decomposition) and 149-52° (decomposition), resp.

IT **89534-10-1**, Phosphorodiamidic acid, [4-amino-2-(methylthio)-5-pyrimidinyl]methyl ester **90222-55-2**, Phosphorodiamidic acid, N,N'-dimethyl-, [4-amino-2-(methylthio)-5-pyrimidinyl]methyl ester
(preparation of)

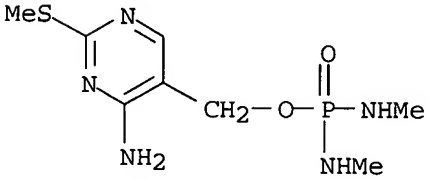
RN 89534-10-1 CAPLUS

CN Phosphorodiamidic acid, [4-amino-2-(methylthio)-5-pyrimidinyl]methyl ester (7CI) (CA INDEX NAME)



RN 90222-55-2 CAPLUS

CN Phosphorodiamidic acid, N,N'-dimethyl-, [4-amino-2-(methylthio)-5-pyrimidinyl]methyl ester (7CI) (CA INDEX NAME)



=> d l17 ibib abs hitstr tot

L17 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:761756 CAPLUS

DOCUMENT NUMBER: 126:42673

TITLE: Tumor protease-activated prodrugs of phosphoramide mustard analogs as antitumor agents

INVENTOR(S): Glazier, Arnold
PATENT ASSIGNEE(S): Drug Innovation & Design, Incorporated, USA; Glazier, Arnold
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9633198	A1	19961024	WO 1996-US4882	19960411 <--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
US 5659061	A	19970819	US 1995-425477	19950420 <--
CA 2215264	AA	19961024	CA 1996-2215264	19960411 <--
AU 9655389	A1	19961107	AU 1996-55389	19960411 <--
AU 697110	B2	19980924		
EP 821689	A1	19980204	EP 1996-912645	19960411 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11504009	T2	19990406	JP 1996-531791	19960411 <--
AT 202781	E	20010715	AT 1996-912645	19960411
ES 2160815	T3	20011116	ES 1996-912645	19960411
PT 821689	T	20011228	PT 1996-912645	19960411
GR 3036796	T3	20020131	GR 2001-401658	20011004

PRIORITY APPLN. INFO.: US 1995-425477 A 19950420
WO 1996-US4882 W 19960411

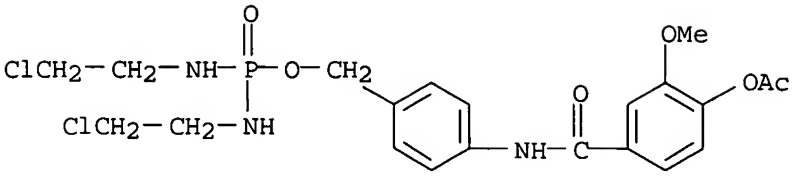
OTHER SOURCE(S): MARPAT 126:42673

AB The composition, synthesis, and applications of tumor-associated protease-activated prodrugs of phosphoramide mustard, isophosphoramide mustard, and analogs with detoxification functionalities are described. These drugs release a cytotoxic phosphoramide mustard analog following activation by tumor-associated proteases and esterases. The general structure for these drugs is AP(O)R1R2 (I) [R1 = (substituted) NHCH2CH2X; X = leaving group; R2 = (substituted) amino, (substituted) NHCH2CH2X; A = benzyloxy with ≥1 acyloxy or acylamino groups para or ortho to the phosphoester, wherein the acyloxy or acylamino groups are not (substituted or unsubstituted) p-guanidinobenzoyloxy or p-guanidinobenzoylamino groups]. **Thus**, I (A = 4-acetoxy-3-methoxybenzyloxy; R2 = NHCH2CH2X; X = Cl) (V-Isophos) was highly toxic to CEM cells (IC50 = 0.01 μM) and IPC-81 rat myeloid leukemic cells in vitro and to FSA2 mouse fibrosarcomas in vivo, and was less toxic to bone marrow cells than other antitumor agents tested.

IT **184532-57-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tumor protease-activated prodrugs of phosphoramide mustard analogs as antitumor agents)

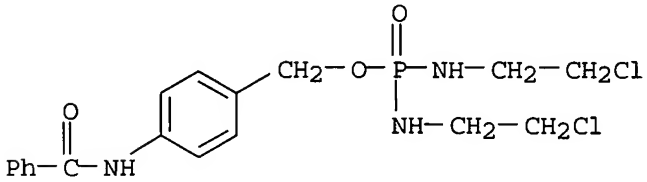
RN 184532-57-8 CAPLUS

CN Phosphorodiamidic acid, N,N'-bis(2-chloroethyl)-, [4-[[4-(acetyloxy)-3-methoxybenzoyl]amino]phenyl]methyl ester (9CI) (CA INDEX NAME)

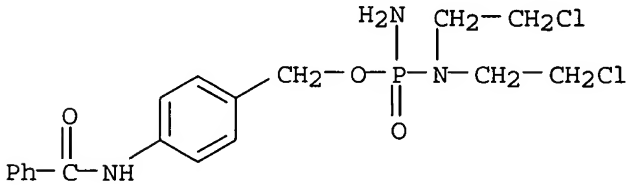


IT **184532-53-4 184532-54-5 184532-55-6 184532-56-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tumor protease-activated prodrugs of phosphoramide mustard analogs as antitumor agents)

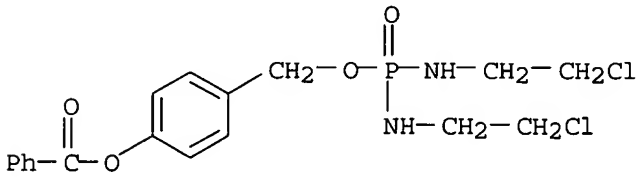
RN 184532-53-4 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-chloroethyl)-, [4-(benzoylamino)phenyl]methyl ester (9CI) (CA INDEX NAME)



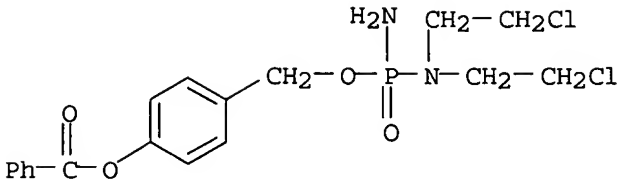
RN 184532-54-5 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, [4-(benzoylamino)phenyl]methyl ester (9CI) (CA INDEX NAME)



RN 184532-55-6 CAPLUS
CN Phosphorodiamidic acid, N,N'-bis(2-chloroethyl)-, [4-(benzoyloxy)phenyl]methyl ester (9CI) (CA INDEX NAME)



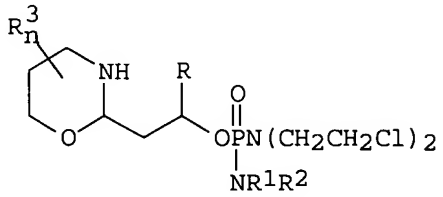
RN 184532-56-7 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, [4-(benzoyloxy)phenyl]methyl ester (9CI) (CA INDEX NAME)



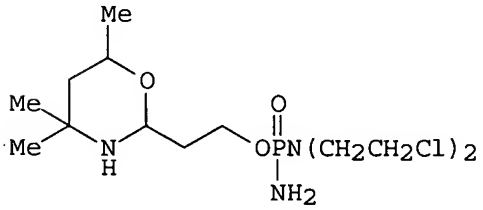
L17 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:572343 CAPLUS
DOCUMENT NUMBER: 113:172343
TITLE: Preparation of aldophosphamides as antitumor agents
INVENTOR(S): Borch, Richard F.; Valente, Ronald R.
PATENT ASSIGNEE(S): Research Corp. Technologies, Inc., USA
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8911283	A1	19891130	WO 1989-US2272	19890523 <--
W: DK, JP				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4908356	A	19900313	US 1988-198429	19880525 <--
CA 1337601	A1	19951121	CA 1989-600535	19890524 <--
PRIORITY APPLN. INFO.:			US 1988-198429 A	19880525

OTHER SOURCE(S): CASREACT 113:172343; MARPAT 113:172343
GI



I



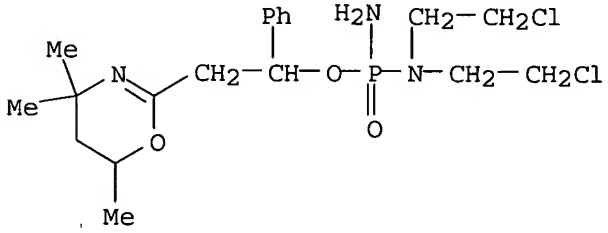
II

AB The title compds. [I; R = H, alkyl, cycloalkyl, arylalkyl, aryl, heterocyclyl, heterocyclylalkyl; R1, R2 = H, (halo-, alkoxy-, or OH-substituted) alkyl; R1R2N = morpholino; R3 = H, alkyl, CO2H alkoxycarbonyl; n = 0-3], were prepared as neoplasm inhibitors (phosphoramide mustard prodrugs). **Thus**, H2C:CHCH2CH2OH was

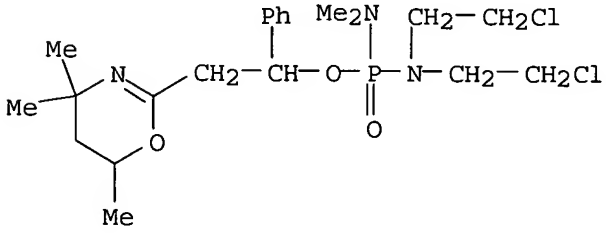
treated successively with BuLi, Cl2P(O)N(CH2CH2Cl)2, and NH3 to give H2C:CHCH2CH2OP(O)(NH2)N(CH2CH2Cl)2. The latter was treated successfully with O3, Me2S, and H2NCMe2CH2CHMeOH/K2CO3 to give II. I had LC99 (concentration for 99% kill) of 5-145 μM against cyclophosphamide-resistant L1210 tumor cells. I are free of the urinary bladder toxicity shown by cyclophosphanides.

IT **129904-24-1P 129904-25-2P 129904-27-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of, in preparation of neoplasm inhibitor)

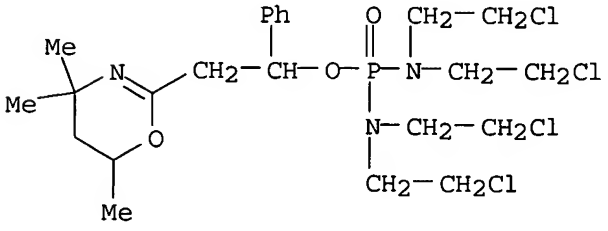
RN 129904-24-1 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, 2-(5,6-dihydro-4,4,6-trimethyl-4H-1,3-oxazin-2-yl)-1-phenylethyl ester (9CI) (CA INDEX NAME)



RN 129904-25-2 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-N',N'-dimethyl-, 2-(5,6-dihydro-4,4,6-trimethyl-4H-1,3-oxazin-2-yl)-1-phenylethyl ester (9CI) (CA INDEX NAME)



RN 129904-27-4 CAPLUS
CN Phosphorodiamidic acid, tetrakis(2-chloroethyl)-, 2-(5,6-dihydro-4,4,6-trimethyl-4H-1,3-oxazin-2-yl)-1-phenylethyl ester (9CI) (CA INDEX NAME)

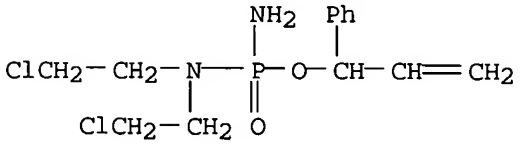


IT **129904-22-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of, as intermediate for oxazinylethylphosphorodiamidate neoplasm inhibitor)

RN 129904-22-9 CAPLUS

CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, 1-phenyl-2-propenyl ester (9CI) (CA INDEX NAME)



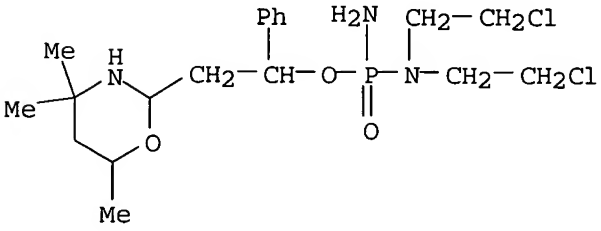
IT **129904-18-3P 129904-19-4P 129904-21-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of, as neoplasm inhibitor)

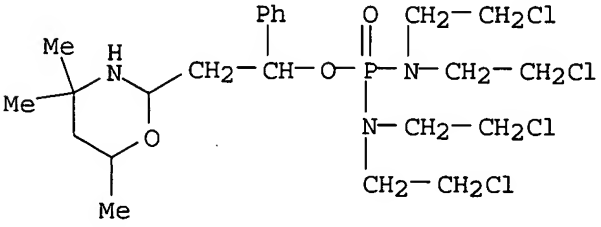
RN 129904-18-3 CAPLUS

CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, 1-phenyl-2-(tetrahydro-4,4,6-trimethyl-2H-1,3-oxazin-2-yl)ethyl ester (9CI) (CA INDEX NAME)



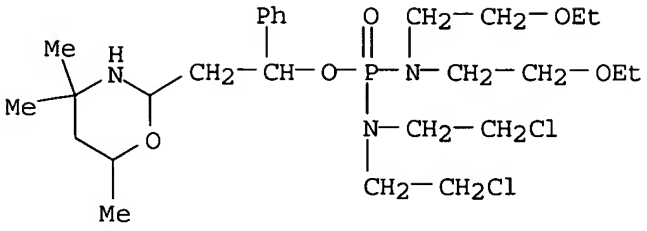
RN 129904-19-4 CAPLUS

CN Phosphorodiamidic acid, tetrakis(2-chloroethyl)-, 1-phenyl-2-(tetrahydro-4,4,6-trimethyl-2H-1,3-oxazin-2-yl)ethyl ester (9CI) (CA INDEX NAME)



RN 129904-21-8 CAPLUS

CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-N',N'-bis(2-ethoxyethyl)-, 1-phenyl-2-(tetrahydro-4,4,6-trimethyl-2H-1,3-oxazin-2-yl)ethyl ester (9CI) (CA INDEX NAME)

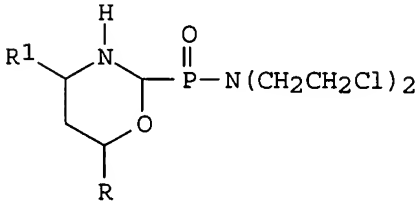


L17 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:526596 CAPLUS
DOCUMENT NUMBER: 113:126596
TITLE: Cyclophosphamide analogs useful as antitumor agents
INVENTOR(S): Borch, Richard F.; Canute, Gregory W.
PATENT ASSIGNEE(S): Research Corp. Technologies, Inc., USA
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2

DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8911278	A1	19891130	WO 1989-US2238	19890523 <--
W: DK, JP				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 5190929	A	19930302	US 1988-198406	19880525 <--
PRIORITY APPLN. INFO.:			US 1988-198406	A 19880525

OTHER SOURCE(S): MARPAT 113:126596
GI

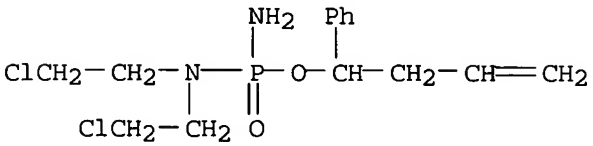


I

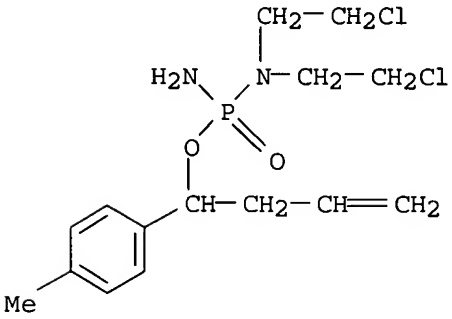
AB Cyclophosphamide analogs I (R = lower alkyl, aryl, aryl-lower alkyl, or N-, S-, or O-containing heterocycle; R1 = H, OH, OOH; when R1 = H, R ≠ Me, Ph; when R1 = OH, R ≠ Me) and their salts are useful as neoplasm inhibitors. **Thus**, 1-p-tolyl-3-butenyl N,N-bis(2-chloroethyl)phosphorodiamidate (preparation described) 18.56 mM was dissolved in Me2CO/H2O, treated with O3 for 30 min at 0°, flushed with O2, and reacted with H2O2 overnight. Workup yielded I (R1 = OOH; R = p-tolyl) (II). II injected i.p. at 60 μmol/kg increased the survival time of L1210 tumor-bearing mice 180%.

IT **129253-37-8P 129253-39-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of cyclophosphamide analog neoplasm

inhibitor)
RN 129253-37-8 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, 1-phenyl-3-butenyl ester (9CI) (CA INDEX NAME)



RN 129253-39-0 CAPLUS
CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, 1-(4-methylphenyl)-3-butenyl ester (9CI) (CA INDEX NAME)

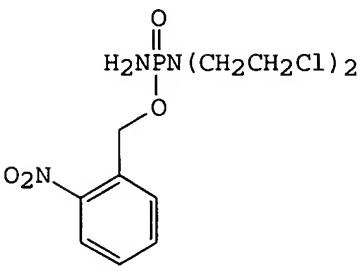


L17 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:198797 CAPLUS
DOCUMENT NUMBER: 112:198797
TITLE: Phosphoramides useful as antitumor agents
INVENTOR(S): Borch, Richard F.; Canute, Gregory W.; Valente, Ronald R.
PATENT ASSIGNEE(S): Research Corp. Technologies, Inc., USA
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 8911484	A1	19891130	WO 1989-US2299		19890525	<--
W: DK, JP						
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE						
EP 418292	A1	19910327	EP 1989-906634		19890525	<--
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE						
JP 04501253	T2	19920305	JP 1989-506400		19890525	<--
US 5403932	A	19950404	US 1994-260040		19940615	<--
PRIORITY APPLN. INFO.:			US 1988-198408	A	19880525	
			WO 1989-US2299	W	19890525	
			US 1991-741930	B1	19910808	

OTHER SOURCE(S): MARPAT 112:198797

GI



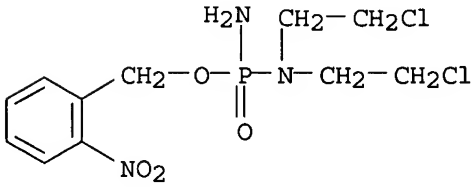
II

AB R1R2NP(O)(OCHRCHR3R4)N(CH2CH2Cl)2 [I; R = nitroaryl, nitroheteroaryl; R1, R2 = H, (halo-, OH-, or alkoxy-substituted) alkyl; R1R2N = morpholino; R3, R4 = H, electron-withdrawing group, (alkyl- or electron-withdrawing-group-substituted) alkyl], were prepared **Thus**, 2-O2NC6H4CH2OH in THF at 0° was treated with BuLi and the mixture was added to Cl2P(O)N(CH2CH2Cl)2 (preparation given) in THF. The mixture was stirred 1 h at 0°, NH3 was added, and stirring was continued for 1 h to give 26% II. I had LC99 of 123-350 μM against cyclophosphamide-sensitive L1210 cells. I are said to be free of the urinary bladder toxicity exhibited by cyclophosphamide and are effective against cyclophosphamide-resistant tumors.

IT **126893-93-4P 126893-94-5P 126893-95-6P 126893-96-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as neoplasm inhibitor)

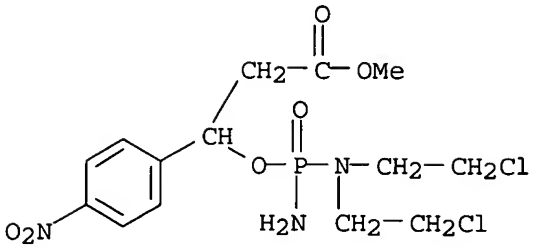
RN 126893-93-4 CAPLUS

CN Phosphorodiamidic acid, N,N-bis(2-chloroethyl)-, (2-nitrophenyl)methyl ester (9CI) (CA INDEX NAME)

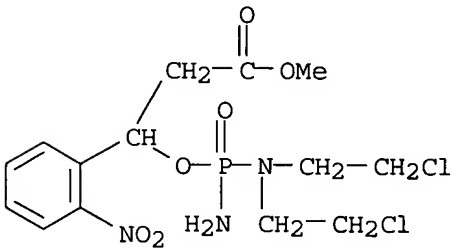


RN 126893-94-5 CAPLUS

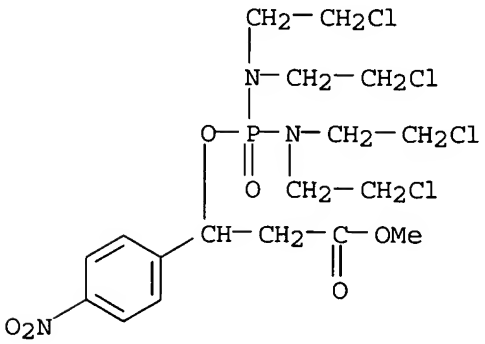
CN Benzenepropanoic acid, β-[[amino[bis(2-chloroethyl)amino]phosphinyl]oxy]-4-nitro-, methyl ester (9CI) (CA INDEX NAME)



RN 126893-95-6 CAPLUS
CN Benzenepropanoic acid, β-[[amino[bis(2-chloroethyl)amino]phosphinyl]oxy]-2-nitro-, methyl ester (9CI) (CA INDEX NAME)



RN 126893-96-7 CAPLUS
CN Benzenepropanoic acid, β-[[bis[bis(2-chloroethyl)amino]phosphinyl]oxy]-4-nitro-, methyl ester (9CI) (CA INDEX NAME)



L17 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1985:61449 CAPLUS
DOCUMENT NUMBER: 102:61449
TITLE: Urease-inhibited urea based fertilizer compositions containing phosphorus compounds
INVENTOR(S): Swerdloff, Michael Dennis; Van der Puy, Michael; Kolc, Jaroslav Fitzgerald; Rogic, Milorad Mihailo; Anello, Louis Gene; Hendrickson, Larry Lee
PATENT ASSIGNEE(S): Allied Corp., USA
SOURCE: Eur. Pat. Appl., 49 pp.
CODEN: EPXXDW

DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

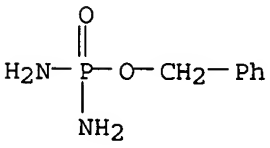
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 119494	A1	19840926	EP 1984-101739	19840220 <--
R: DE, FR, GB, IT, NL				
US 4517002	A	19850514	US 1983-475989	19830316 <--
US 4539037	A	19850903	US 1983-475990	19830316 <--
US 4540428	A	19850910	US 1983-475980	19830316 <--
AU 8425658	A1	19840920	AU 1984-25658	19840315 <--
AU 574667	B2	19880714		
CA 1236702	A1	19880517	CA 1984-449663	19840315 <--

PRIORITY APPLN. INFO.:
US 1983-475980 A 19830316
US 1983-475989 A 19830316
US 1983-475990 A 19830316

AB Improved fertilizer compns. comprise urea and(or) ≥1 urea precursor and a urease [9002-13-5]-inhibiting P compound of the formula (NR1R2)P:X(NR3R4)R5 (X = O or S; R1, R2, R3, and R4 = H or C1-4 alkyl; R5 = NR6R7, OR8, or NR9R10; R6,R8 = alkyl, etc.; R7 = e.g., heterocycle; R9 = substituted alkyl; R10 = R9, H, cycloalkenyl, etc.). **Thus**, N-methyl-N-(4-nitrophenyl)phosphoramidic dichloride [94511-60-1] was prepared by heating p-nitro-N-methylaniline [100-15-2] and POCl3 and was then reacted with NH3 in CH2Cl2. The N-methyl-N-(4-nitrophenyl)phosphoric triamide [94511-45-2] obtained by filtration was an excellent urease inhibitor even when soil temps. were 35° for 12 days, whereas the known inhibitor Ph phosphorodiamidate allowed complete urea hydrolysis after only 6 days at 35°.

IT **86197-91-3P**
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); BIOL (Biological study); PREP (Preparation); USES (Uses)
(urease inhibitor, preparation and efficacy of)

RN 86197-91-3 CAPLUS
CN Phosphorodiamidic acid, phenylmethyl ester (9CI) (CA INDEX NAME)



L17 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1978:508644 CAPLUS
DOCUMENT NUMBER: 89:108644
TITLE: Phosphoroamidates
INVENTOR(S): Morgan, Albert W.; Schumacher, Ignatius; Vanderlinde, William
PATENT ASSIGNEE(S): Monsanto Co., USA
SOURCE: U.S., 11 pp.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

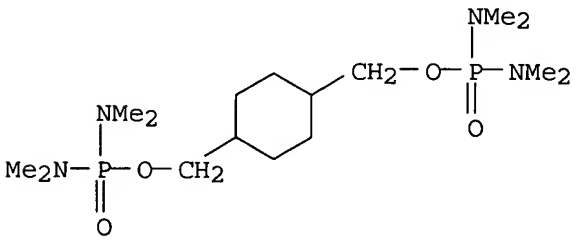
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4086302	A	19780425	US 1976-727913	19760929 <--
US 4144394	A	19790313	US 1977-862080	19771219 <--
PRIORITY APPLN. INFO.:			US 1972-276810 A2	19720731
			US 1974-459257 A3	19740408
			US 1975-599569 A2	19750728

AB ZOP(Z1)(NRR1)2 and Z[OP(Z1)(NRR1)2]n [Z = residue of a hydroxyl-containing moiety; Z1 = O, S; R,R1 = individual same or different alkyl, cycloalkyl, aryl; or NRR1 = 5 or 6 membered O, S, or N containing heterocyclyl; n = 2 or greater and is equal to the number of OH groups in the original hydroxyl-containing moiety], useful as flame retardants for natural and synthetic polymeric materials, were prepared by treating phosphorohalidates with amines. **Thus**, bisphenol A was refluxed with POCl3 in the presence of pyridine and the resultant bisphosphorodichloridate was treated with Me2NH in the presence of aqueous NaOH to give [p-[(Me2N)2P(O)O]C6H4]2CMe2 (I). In a flame retarding test on an epoxy resin containing 5 parts I/100 parts resin the volatility loss was 0.01%, tensile strength 3200 psi, and O index 22.0 (0 %).

IT **51963-69-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 51963-69-0 CAPLUS

CN Phosphorodiamidic acid, tetramethyl-, 1,4-cyclohexanediylbis(methylene) ester (9CI) (CA INDEX NAME)



L17 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1977:425818 CAPLUS
DOCUMENT NUMBER: 87:25818
TITLE: Improved hydraulic liquids
INVENTOR(S): Heber, John F.
PATENT ASSIGNEE(S): Monsanto Co., USA
SOURCE: Ger. Offen., 34 pp.
CODEN: GWXXBX
DOCUMENT TYPE: **Patent**
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2625878	A1	19761223	DE 1976-2625878	19760609 <--
US 4056480	A	19771101	US 1975-585636	19750610 <--
NL 7606145	A	19761214	NL 1976-6145	19760608 <--
JP 51149884	A2	19761223	JP 1976-66639	19760609 <--

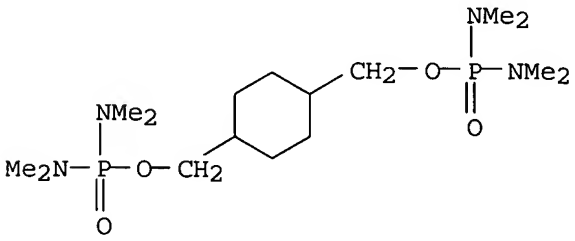
FR 2314243	A1	19770107	FR 1976-17415		19760609 <--
GB 1532904	A	19781122	GB 1976-23851		19760609 <--
AU 507315	B2	19800214	AU 1976-14748		19760609 <--
PRIORITY APPLN. INFO.:			US 1975-585636	A	19750610

AB Diphosphate esters and amidates [R[O2PXY]2, where R = oxydiethylene, 1,4-cyclohexylenedimethylene, or isopropylidenedi-1,4-cyclohexylene; and X,Y = OBu, NMe2, 2-ethylhexyloxy, or cyclohexyloxy] are prepared for use as hydraulic fluids. **Thus**, to 307 g POCl3 at 20°/500 mm was added 106 g (HOCH2CH2)2O over 4 h with reduction in pressure to 80 mm, giving 333.5 g (Cl2PO2CH2CH2)2O (I) [53461-81-7], which was added over 1-2 h to 741.2 g BuOH at 20° to provide 355 g diethylene glycol bis(dibutyl phosphate) [62955-03-7]. Similar prepns. were given for 12 other esters, amidates, and acid chlorides.

IT **51963-69-0P**
RL: PREP (Preparation)
(manufacture of, as hydraulic fluids)

RN 51963-69-0 CAPLUS

CN Phosphorodiamidic acid, tetramethyl-, 1,4-cyclohexanediylbis(methylene) ester (9CI) (CA INDEX NAME)



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=> log y
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                                                 ENTRY    SESSION
FULL ESTIMATED COST                              76.37     578.86

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                 ENTRY    SESSION
CA SUBSCRIBER PRICE                              -9.49     -10.95

STN INTERNATIONAL LOGOFF AT 14:32:16 ON 31 MAY 2005
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